THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY

VOL. 63 JUNE, 1950 No. 6

STANNIC OXIDE PNEUMOCONIOSIS

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PNEUMOCONIOSIS due to tin oxide was regarded as a clinical entity in 1948 by Pendergrass and Pryde[17] who reported 1 case in a worker exposed to the dust for fifteen years while bagging tin oxide. Cutter *et al.*[5] reported 2 cases in 1949 who had about twenty years' exposure to tin oxide dust in a tin oxide recovery plant. One of the patients who operated the calcining furnace had considerable additional exposure to furnace fumes and the possibility that the fumes constituted a special exposure hazard was mentioned. The chest roentgenograms of patients with stannic oxide pneumoconiosis show discrete shadows 1 mm. to 2 mm. in size and of great radiopacity, scattered uniformly throughout the lungs. The shadows have been attributed to stannic oxide deposits in the lungs; however, no morphologic description of the lungs has been published in the English literature. The patients reported above are living with no evidence of impaired pulmonary function or systemic disease.

Seven cases of "pulmonary stannosis" were reported in Prague, Czechoslovakia by Bartak *et al.*[2] in 1948. According to an abstract of this article, the workers operated a furnace in which tin was "burned" to tin oxide, and were exposed to furnace fumes as well as to tin oxide dust. It was impossible to obtain a complete translation of this paper; however, one of the patients died of carcinoma of the stomach and autopsy findings were reported.

A patient admitted to Lakeside Hospital with carcinoma of the prostate was found to have a chest roentgenogram suggestive of an unusual type of pneumoconiosis. There was a history of an eighteen year industrial exposure to tin oxide. Clinical, autopsy and analytical studies of this case are reported. When the striking roentgenographic appearance of stannic oxide pneumoconiosis is more widely known, additional cases will be recognized. Industrial roentgen surveys and mass chest roentgen surveys will uncover cases in patients who have no symptoms and have not sought medical care. It is important to prove that the condition is a "benign pneumoconiosis" as indicated by Pendergrass and Pryde.[17]

REPORT OF CASE

A white male handy man, aged seventy-two, first entered Lakeside Hospital on September 23,

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1948, complaining of constant lower abdominal pain of two weeks' duration, nocturia and rapid loss of weight.

Occupational and Past Medical History. The man had been employed in industry from 1912 until 1930. During this entire period of eighteen years he tended a detinning furnace in which stannic oxide (SnO_2) was recovered from tin scrap by a calcining process. He was exposed not only to heavy furnace fumes, but also to much dust from the finished product, a heavy white powder. At no time during or after the period of exposure did he have symptoms of respiratory disease.

In 1939, nine years after his last exposure, he was admitted to another hospital because of epigastric pain and vomiting. He improved on symptomatic therapy. A roentgenogram of the chest made at that time had a "peculiar widespread mottling of both lung fields by discrete shadows." These findings were thought to be consistent with fungous disease. There were no respiratory complaints, however, and no fungi or acid-fast organisms were recovered from the sputum.

On admission the temperature was 38.4° C., pulse 96, respirations 24, and blood pressure 160/100. The thorax was moderately increased in anteroposterior diameter. There was sharp pain in the lower left side of the chest on deep inspiration. The lungs and heart were normal on percussion and auscultation. Vital capacity was 3,600 cc., or 85 per cent of normal. The abdomen was tense, and there was unlocalized tenderness in the lower quadrants. The neurological examination was negative. The prostate was enlarged, irregular and firm, with a fixed and indurated base. The seminal vesicles were firm, and the left nodular.

The hemoglobin content of the blood was 10 grams per 100 cc., leukocyte count 11,000, blood urea nitrogen 29 milligrams per 100 cc., serum acid phosphatase 10.0 Bodansky units per 100 cc. The urine specific gravity was 1.010, and showed a trace of albumin. The blood Kline reaction was negative.

Roentgenographic Examination. Chest: "The lungs are involved by discrete shadows that have the density of lipiodol droplets and vary in size from less than 1 mm. to about 2 mm. The shadows are evenly scattered throughout the lungs 2 mm. to 4 mm. apart. There is no evidence of enlarged hilar lymph nodes. The heart is moderately enlarged. There is a pathologic fracture of the left 10th rib" (Fig. 1).

Pelvis: "Bone destructive processes of left pubic bone and left ischium."

On stilbestrol and penicillin therapy the pain disappeared, the prostate decreased in size and the temperature became normal. On the seventh hospital day partial left pneumothorax was discovered on physical examination. Two days later a roentgenogram of the chest revealed collapse of an estimated 15 per cent of the left lung, chiefly at the apex and base. It was thought that pleural adhesions to the mid-portion of the left lateral thoracic wall in the region of the fractured rib had partially maintained the position of the lung. The lung gradually re-expanded.

The patient was readmitted six months later complaining of aching pain in the back. He was febrile, and there were signs of consolidation over the left side of the chest posteriorly. On the roentgenogram there was a small area of increased density in the lower portion of the left lower lobe, in addition to the diffuse mottling of both lungs noted on the previous admission. On penicillin therapy the fever subsided. Serial chest roentgenograms showed considerable resolution of the pneumonia by the tenth day, but a hazy density of the peripheral portion of the affected lobe in the region of the previously described pathological rib fracture still persisted at the time of discharge from the hospital on the twentieth day.

The final admission was six weeks later. Weakness, lethargy and emaciation had gradually increased. There were moist rales over the lower left chest posteriorly. The blood urea nitrogen was 174 milligrams per 100 cc. Small amounts of cloudy urine obtained by catheter had numerous leukocytes in the sediment. The patient died on the fourth hospital day.

AUTOPSY. Permission for examination was limited to thorax and abdomen.

The body was that of a normally developed, markedly emaciated white male, whose appearance was consistent with the stated age of seventy-three years. There were no significant abnormalities of the head or neck. The thorax was symmetrical and moderately increased in anteroposterior dimension. Dissection disclosed a primary carcinoma of the prostate with extension to the seminal vesicles, the posterior wall of the urinary bladder, and the left ureter with hydroureter and hydronephrosis. There were metastases to lymph nodes, liver, lungs, ribs, lumbar and sacral vertebrae, and to the left innominate bone. These skeletal metastases

were osteolytic. There was an old non-united fracture at the site of a metastasis in the left tenth rib. In the pleura and parenchyma of each lung there were occasional widely scattered metastases averaging 0.5 cm. in diameter. The heart weighed 345 grams and there was no disproportion in the size of the chambers. The kidneys weighed 70 grams and 80 grams, right and left respectively, and were the seat of chronic pyelonephritis. The liver and spleen had scattered microscopic accumulations of black granular pigment in reticulo-endothelial cells. The other significant findings were limited to the respiratory system.

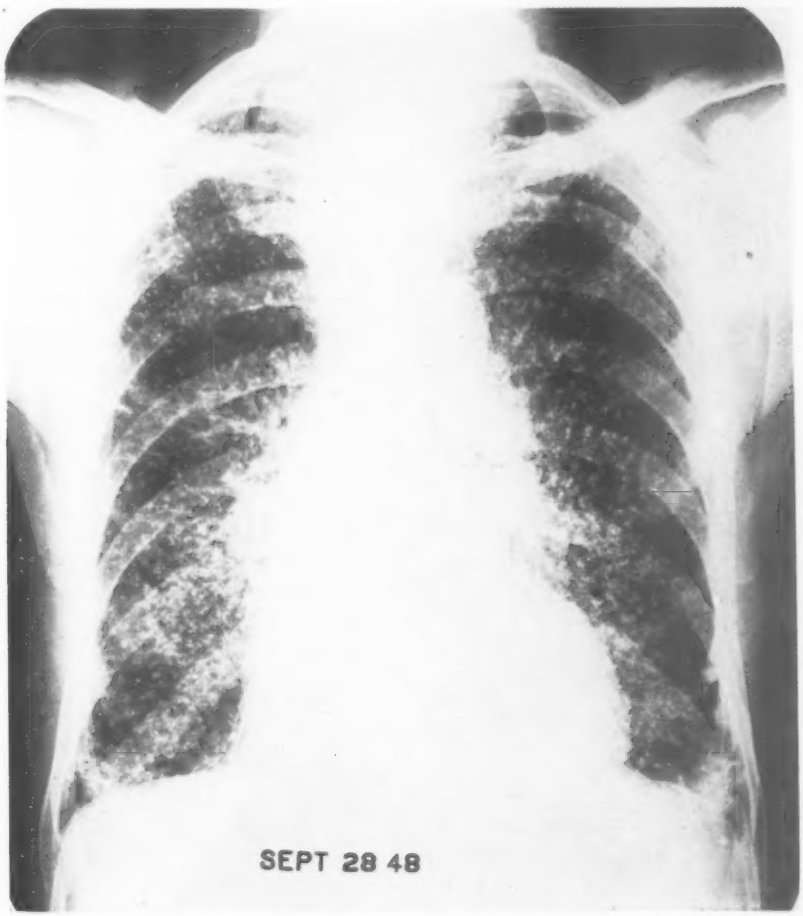

FIG. 1. Male, aged seventy-two, exposed to stannic oxide dust and fumes for eighteen years. Exposure terminated 1930. No respiratory complaints. Uniform distribution of dense discrete shadows throughout both lungs. Moderate cardiac enlargement.

Respiratory System. The thorax was opened under water and contained no extrapulmonary air. There was an estimated 50 cc. of clear yellow fluid in each pleural cavity. There were a few thin pale gray fibrous adhesions between visceral and parietal pleura on the posterior aspect of the upper and middle lobes of the right lung, and in the fissure separating these lobes. The pleural space surrounding the lower lobe of the left lung was almost completely obliterated by visceroparietal, interlobar, pleuropericardial and pleurophrenic dense gray fibrous adhesions. The lower lobe of the right lung and the upper lobe of the left lung were free of adhesions. The lungs weighed 720 grams and 900 grams, right and left respectively. The pleural surfaces, where not involved by fibrous tags, were smooth, glistening and uniformly pinkish gray, traversed by a fine network of black lines. Both lungs were buoyant.

All of the left lower and a small portion of the right upper lobes were the seat of broncho-

pneumonia. Otherwise the lungs were soft, crepitant and normally compressible. The cross section of the formalin-fixed organs (Fig. 2) was gray and uniformly soft with a moderately coarse honeycomb appearance, the individual spaces averaging from 1 to 3 mm. in diameter. Each space was surrounded by a narrow irregular zone of dark gray to black pigmentation. This pattern was most striking in the upper lobes. The largest spaces and the deepest pigmentation occurred in the parenchyma of the apical segments.

Microscopic Description of Lungs. Sections from all lobes of the right lung and from the upper lobe of the left lung were similar. The alveoli were irregularly distended. The interalveolar septa were often thin and frequently interrupted, forming large vesicular spaces. Short spurs with knob-like tips projected into some spaces. Foci of bronchopneumonia were scattered throughout all these lobes and were largest in the right lower lobe. Polymorphonuclear leukocytes were fairly numerous in the alveolar walls in areas not involved by bronchopneumonia. The alveolar walls were frequently the seat of focal histiocytic proliferation. The most conspicuous feature was the presence of particulate dark brown and black pigment distributed throughout the lungs: in alveolar walls and interalveolar septa, at the angular junctions of alveoli, in the interlobular septa, in the peribronchial and perivascular regions, and in the subpleural lymphatics (Fig. 4). Accumulations were heaviest in emphysematous foci. The pigment occurred both as discrete particles and as dense rounded clumps. Where discrete, chiefly in alveolar walls and interalveolar septa,

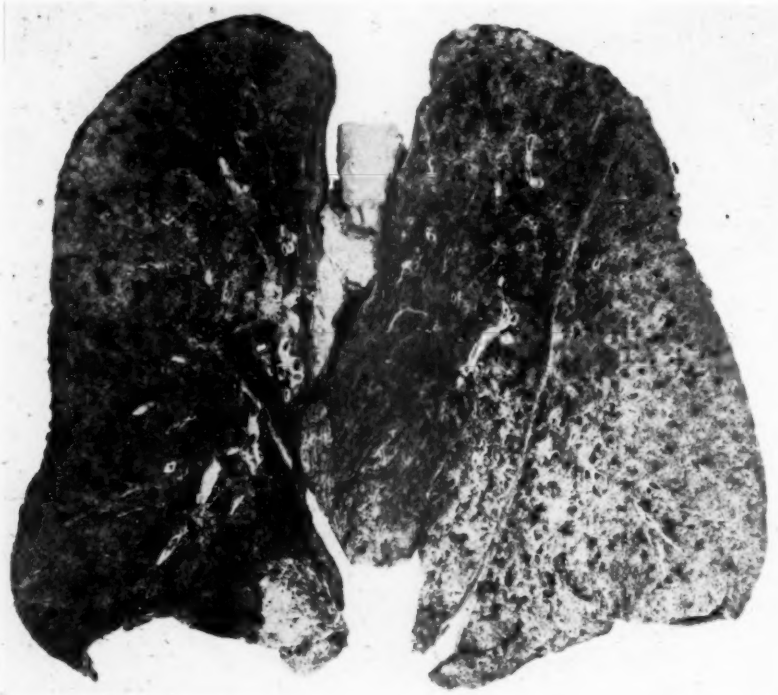

FIG. 2. Coronal section of both lungs after formalin fixation. Black pigmentation of pleura, parenchyma and bronchopulmonary lymph nodes consistent with anthracosis. Chronic pulmonary emphysema, principally of upper lobes; emphysematous pleural blebs on lateral surface of left lower lobe. Organizing pneumonia of left lobe. Bronchopneumonia, widespread.

The bronchopulmonary, paratracheal and other mediastinal lymph nodes measured up to 1.5 cm. in greatest dimension and were moderately soft with a uniformly glistening black section. There were no foci of necrosis, fibrosis or calcification in the nodes. The pulmonary artery and its branches were normal.

A roentgenogram was made of a large wedge-shaped section of the left lung (Fig. 3). This showed dense shadows similar to those observed on the chest roentgenogram. The shadows could now be seen to have chiefly a perivascular, peribronchial and subpleural distribution.

particles measured microscopically by means of a micrometer eyepiece had a range of from 0.5 to 1.6 microns with a mean of 1.0 micron. Most of the particles were granular, but rarely they occurred as spicules which were birefringent under the polarizing microscope. At some sites, notably in the interalveolar septa, the pigment granular non-pigmented cytoplasm. Connective tissue surrounding pigment-choked lymphatics was moderately thickened by loose, rather cellular, pigment-laden collagenous tissue which was lightly infiltrated with large and small mononuclear cells. There was, however, no nodulation or hyalinization (Fig. 6).

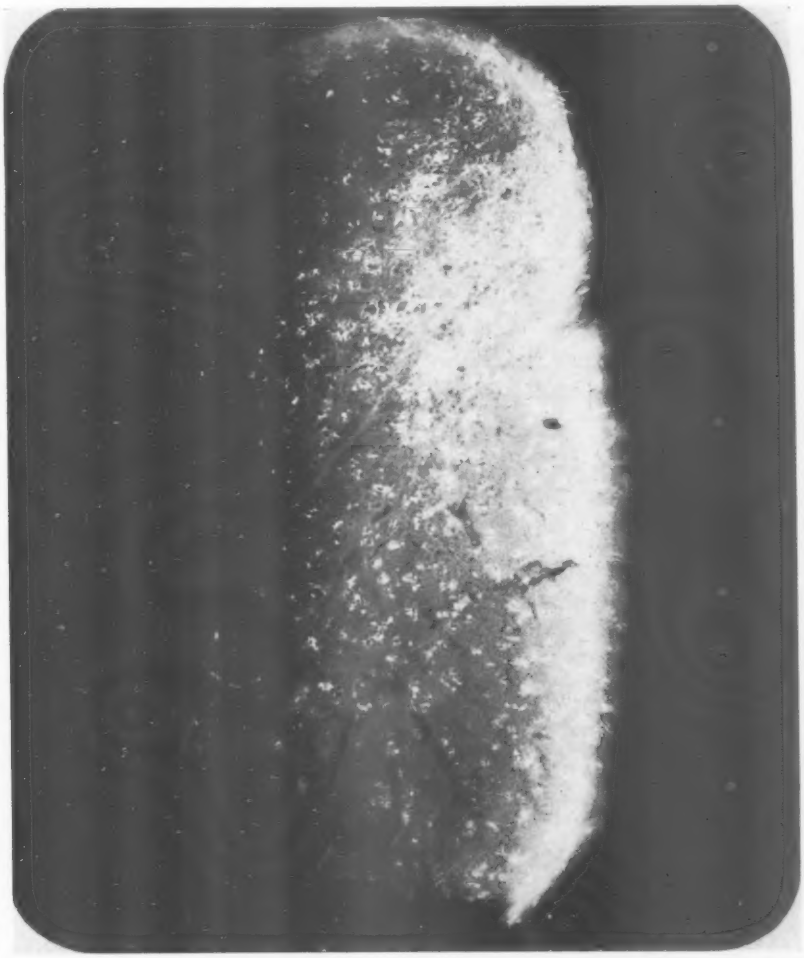

Fig. 3. (×½) Roentgenogram of thin slice of left lung. Specimen wedge-shaped, measuring 2 cm. in thickness at pleural surface (right border), progressively thinner toward central portion. Perivascular, peribronchial and subpleural distribution of radiopaque stannic oxide.

was within phagocytes, frequently obscuring the nucleus. Some of these cells were elongated, and cell outlines often were not distinguishable. Rare pigment-laden macrophages lay free in the alveoli. The densest pigment concentrations were in the perivascular, peribronchial and subpleural lymphatic channels (Fig. 5), which were irregularly dilated and at some sites contained in addition numerous histiocytes with finely

Sections stained with Berlin blue showed a few blue-staining dust-laden macrophages in the lymphatics, and small amounts of pale blue non-granular material diffusely distributed throughout the areolar tissue of the peribronchial and perivascular regions.

Intrapulmonary bronchi had walls of normal thickness and occasionally were the seat of acute catarrhal bronchitis. Some were partially

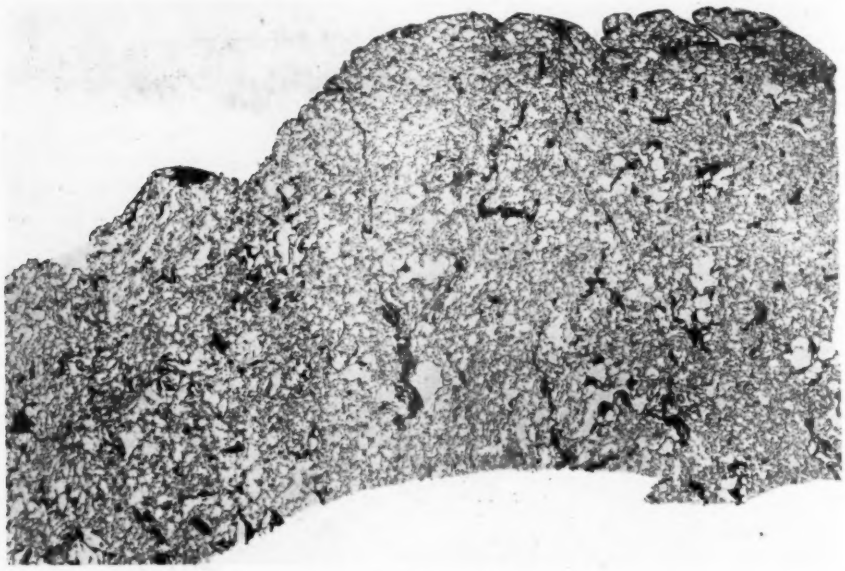

FIG. 4. (×2) Large tissue section of middle lobe of right lung. Chronic pulmonary emphysema, perivascular and peribronchial pigment accumulation, no foci of fibrosis.

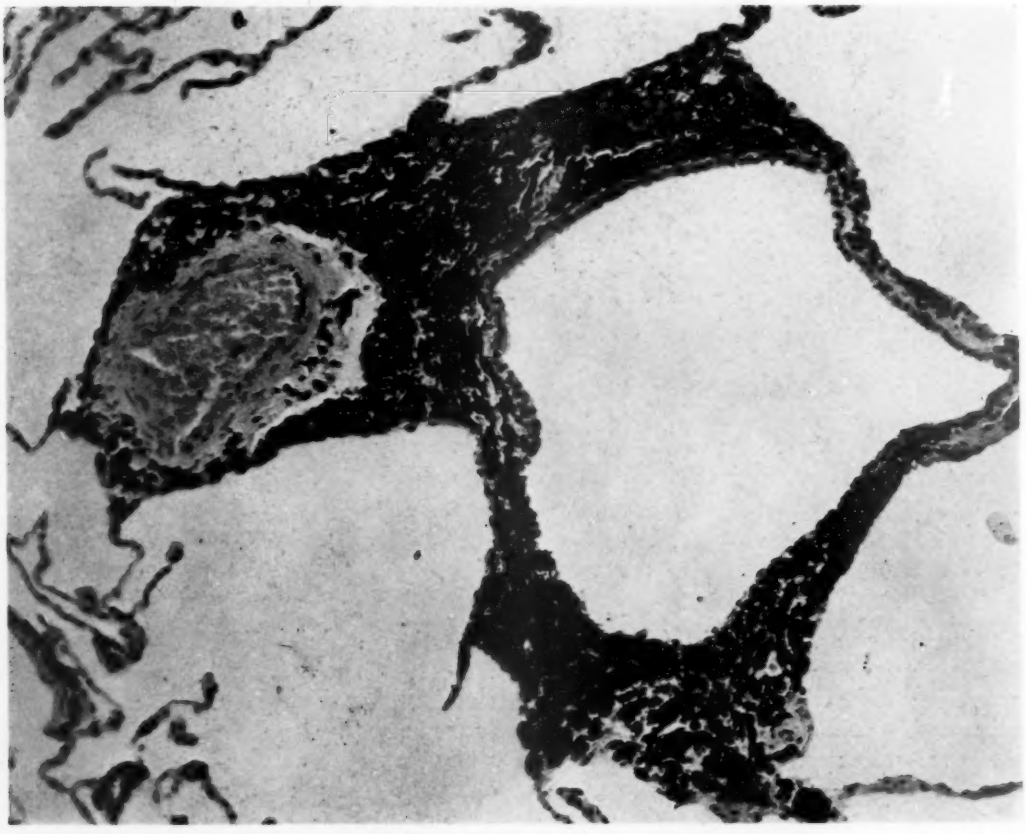

FIG. 5 (×160) Slight thickening of periarterial and peribronchiolar lymphatic trunks with pigment accumulation. Slight bronchiolectasis.

desquamated. There were large focal accumulations of black pigment in the region of and lateral to the mucous glands. The peribronchial lymphatic trunks were irregularly dilated and contained not only pigment-laden macrophages, but at some sites numerous histiocytes with finely granular, non-pigmented cytoplasm. The largest intrapulmonary pigment masses occurred at the sites of lymphoid nodules at the bifurcations of bronchi and bronchioles.

lobe black pigmentation was much less striking, although there was some pigment in the same situations as described in the other lobes. Perivascular fibrosis, pleural thickening and thickening of the interlobular septa were, however, more marked. Much of this increase in connective tissue was caused by relatively young, highly vascular, quite cellular tissue which contained very little pigment and was nowhere hyalinized. This young fibrous tissue

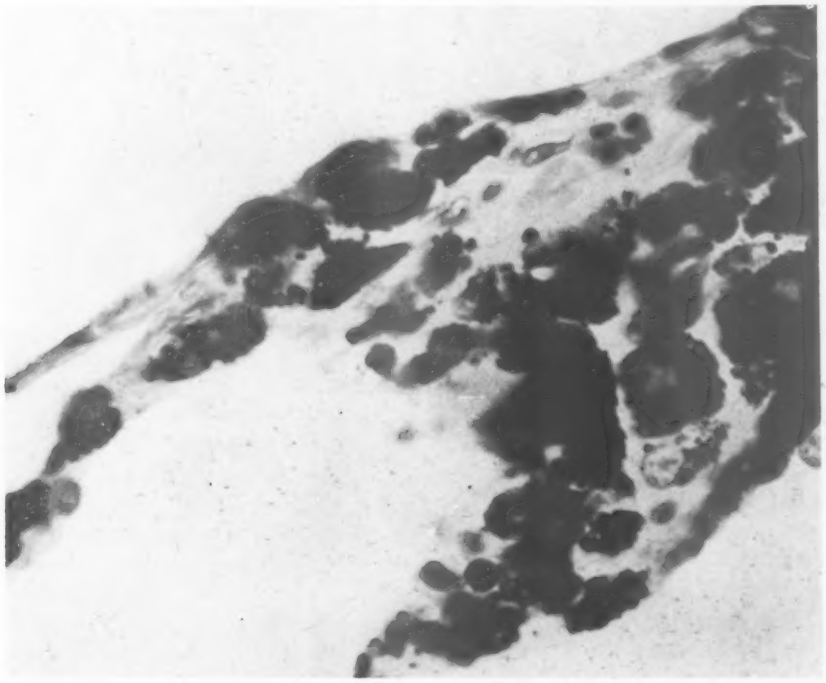

Fig. 6. (×900) Pigment in interlobular septum, occurring as discrete particles within phagocytes, and as compact clumps.

Intrapulmonary veins and larger arteries were normal. Some small arteries in the left upper lobe had slightly thickened walls. Thickening was due to focal subendothelial necrosis and hyalinization. These arteries were surrounded by an increased amount of deeply pigmented collagenous tissue.

Sections of the left lower lobe disclosed a widespread acute bronchopneumonia. In addition, alveoli at many sites contained large irregular isolated masses of organizing fibrin. At some sites organization was complete and the masses were continuous with alveolar walls which were fibrotic. The interalveolar septa were thickened by focal fibrosis and by a preponderance of enlarged septal cells. In this was most abundant in the hilar region of the lobe and surrounded several bronchi which were irregularly compressed, partially desquamated, and acutely and chronically inflamed.

Intrapulmonary veins and large arteries of the left lower lobe were normal. Some small arteries had walls irregularly thickened by intimal hyperplasia, subintimal deposition of lipids and early fibrosis. These arterial changes occurred more frequently and to a more marked degree in the left lower lobe than in other lobes, and were most conspicuous in the foci of connective tissue organization.

The bronchopulmonary and tracheobronchial lymph nodes were similar, though the former

were somewhat more deeply pigmented. The nodes were of normal architecture. Capsules were of normal thickness. The follicles were well preserved. Black pigment was scattered throughout the nodes but was heaviest in the cortex. The pigment occurred chiefly in small rounded clumps and in some instances could be identified as occupying macrophages. These clumps were mostly in the pulp, but there were a few in the peripheral sinuses. Some finely granular pigment lay outside the macrophages, both in the pulp and occasionally in the sinuses. There was a moderate degree of diffuse hyperplasia of the reticular cells. There was no inflammation, necrosis or significant fibrosis of the nodes (Fig. 7).

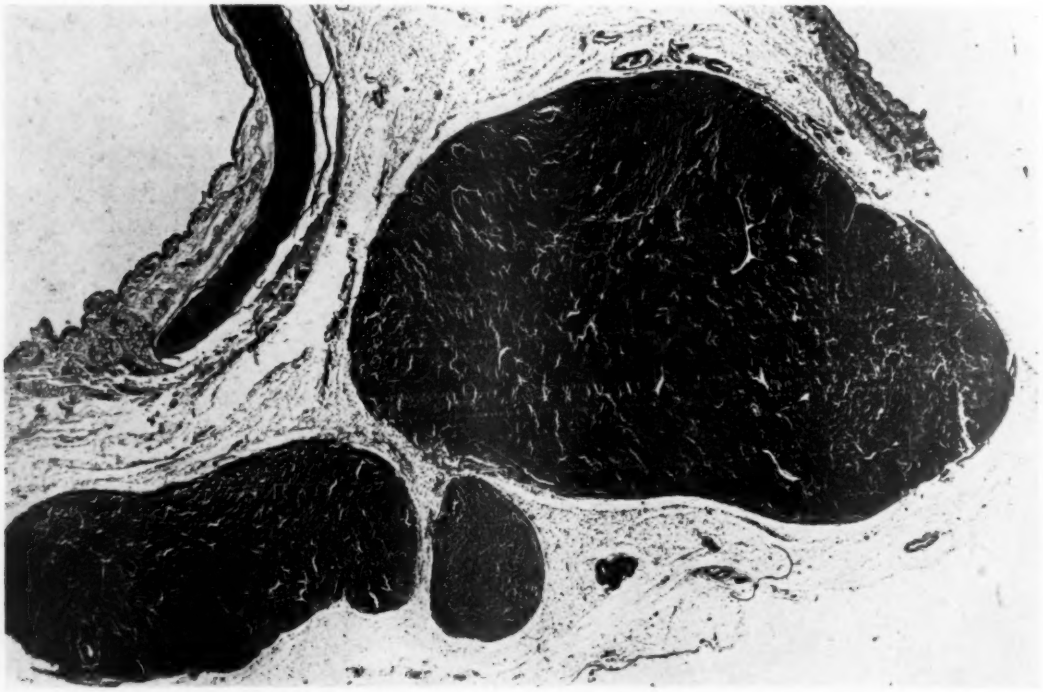

FIG. 7. (×7.5) Tracheobronchial lymph nodes. Not enlarged; black pigmentation; no necrosis or fibrosis.

Anatomic Diagnoses. "Benign" pneumoconiosis; chronic pulmonary emphysema; organizing bronchopneumonia of lower lobe of left lung, with focal fibrosis of interlobular septa; acute bronchopneumonia, widespread; focal bronchiectasis and bronchiolectases; focal acute bronchitis of upper lobe of left lung; arteriosclerosis of small branches of pulmonary artery, marked in lower lobe of left lung; visceroparietal fibrous pleural adhesions of upper and middle lobes of right lung, and of lower lobe of left lung; obliterative interlobar fibrous pleural adhesions of left lung; dust accumulation and reticular hyperplasia of bronchopulmonary and tracheobronchial lymph nodes, moderate; cardiac hypertrophy and dilatation, slight; poorly differentiated adenocarcinoma of the prostate with pelvic extension and widespread metastases; pathologic fracture of left tenth rib; chronic pyelonephritis, bilateral; left hydroureter and hydronephrosis.

Microincineration Studies. Unstained sections of lung mounted on glass slides without cover slips were slowly heated in an electric furnace and held at 550° to 600° C. for one hour according to the method outlined by Irwin.[13] Abundant quantities of fine white powdery ash were produced. Sections from an anthracotic lung treated in the same fashion gave barely visible amounts of grayish-white ash. No trace of black pigment remained in the sections from either case. Microscopically, the tissue pattern was preserved. By comparison with routinely stained adjacent sections cut from the respective paraffin blocks of the stannotic lungs, in the incinerated sections there was an estimated one-third reduction in the amount of particulate matter present in the lymphatic trunks. How-

ever, the relative densities of particle accumulation in the several histoanatomical regions were in the same ratio as those of the black pigment in the stained unincinerated sections. This material now occurred as accumulations of discrete and occasionally agglomerate particles. Similar particles were thinly scattered in the interalveolar and interlobar septa and in the pleura. The individual particles were indistinguishable in size and shape from those described in the stained sections, but with the polarizing microscope all were birefringent, appearing as bright yellowish-brown foci (Fig. 8). These differed in color from the reddish-yellow particles of iron oxide observed in the incinerated sections from a case of a marked pulmonary chronic passive hyperemia, which sections were incinerated along with those of the subject case. Nor did these particles have the brilliant silvery appearance of silica crystals observed in a case of silicosis from which sections were also incinerated.

As a check on the extent to which stannic oxide particles in the lung might be affected by this process of incineration, a bit of commercial-grade white SnO_2 powder was blown across a moist film of Permount on a glass slide and incinerated along with the lung sections. The powder remained unchanged in gross and microscopic appearance.

The incinerated lung sections were flooded with HCl (C.P.) for thirty minutes and gently rinsed with distilled water. The birefringent particles were unaffected. When exposed to HCl in the presence of powdered zinc, however, the particles readily went into solution on the slide. This relative insolubility is characteristic of tin and its oxides. Employing cacotheline as the reagent, a spot test for tin was now made on the acid solution on the slide, and positive result was obtained.

Incinerated sections from an anthracotic lung were treated with HCl in a similar manner. A few discrete particles remaining in the ash

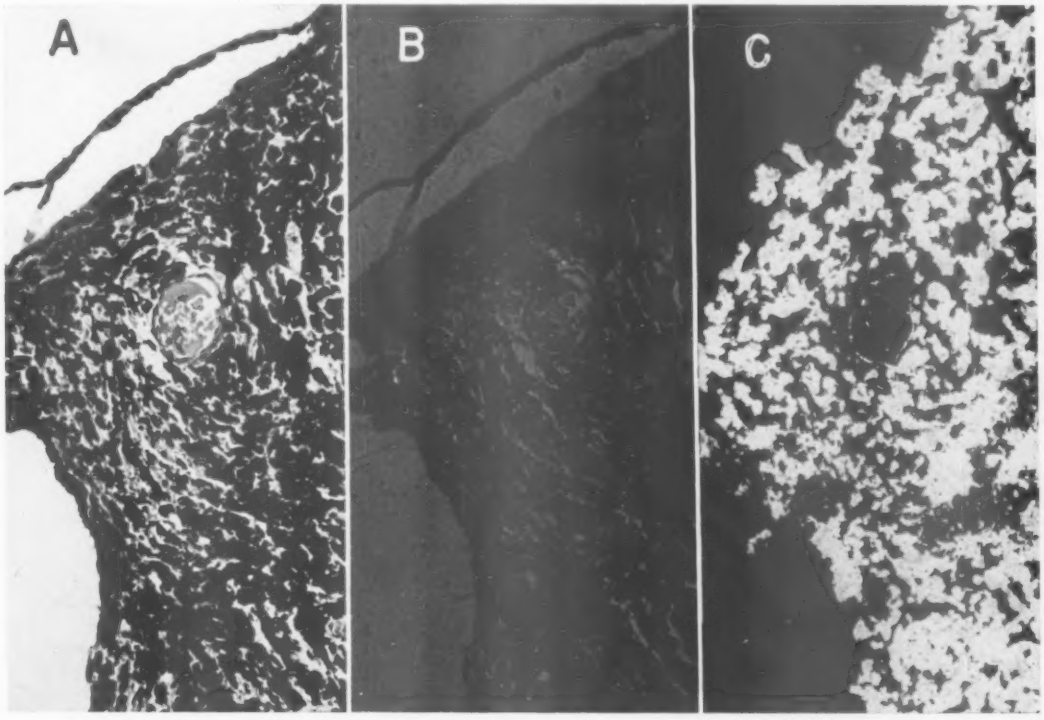

Fig. 8. (×160) Interlobular septum. (*A*) Hematoxylin and eosin stained section, direct illumination. Accumulation of black pigment around small vessel. Indistinguishable from anthracosis. (*B*) Same section, polarized light. No birefringence of particles. (*C*) Adjacent section after microincineration, polarized light. Reduction in perivascular accumulation due to oxidation of carbon particles. Remaining material is highly birefringent, appearing as bright yellowish-brown particles. These gave a positive spot test for tin.

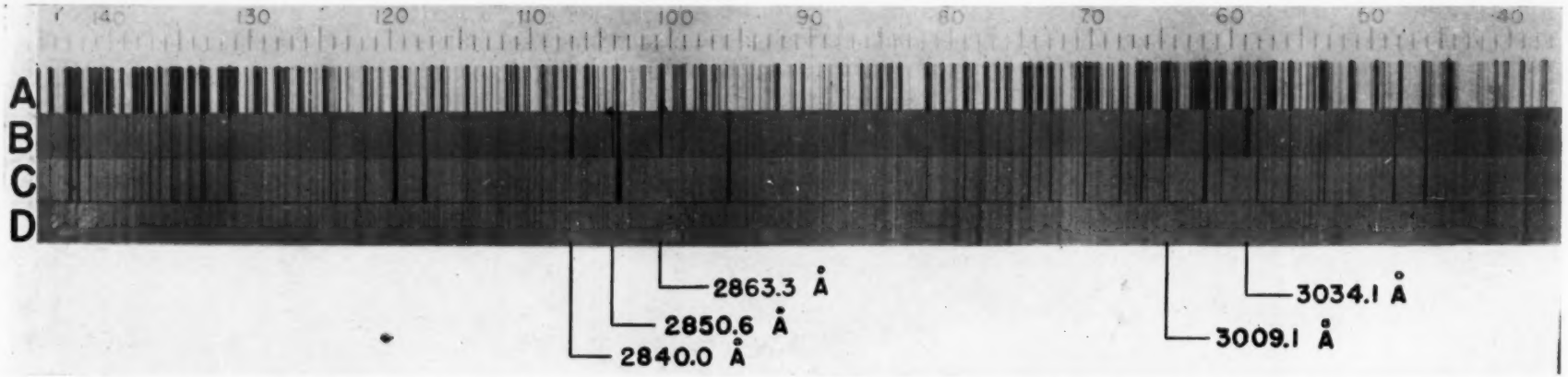

FIG. 9. Spectrogram. The four bands are: (*A*) iron arc; (*B*) lung sample, stannosis; (*C*) control lung sample, anthracosis; (*D*) graphite control. Tin lines on (*B*) are indicated by dots, with wavelengths in Ångström units given beneath.

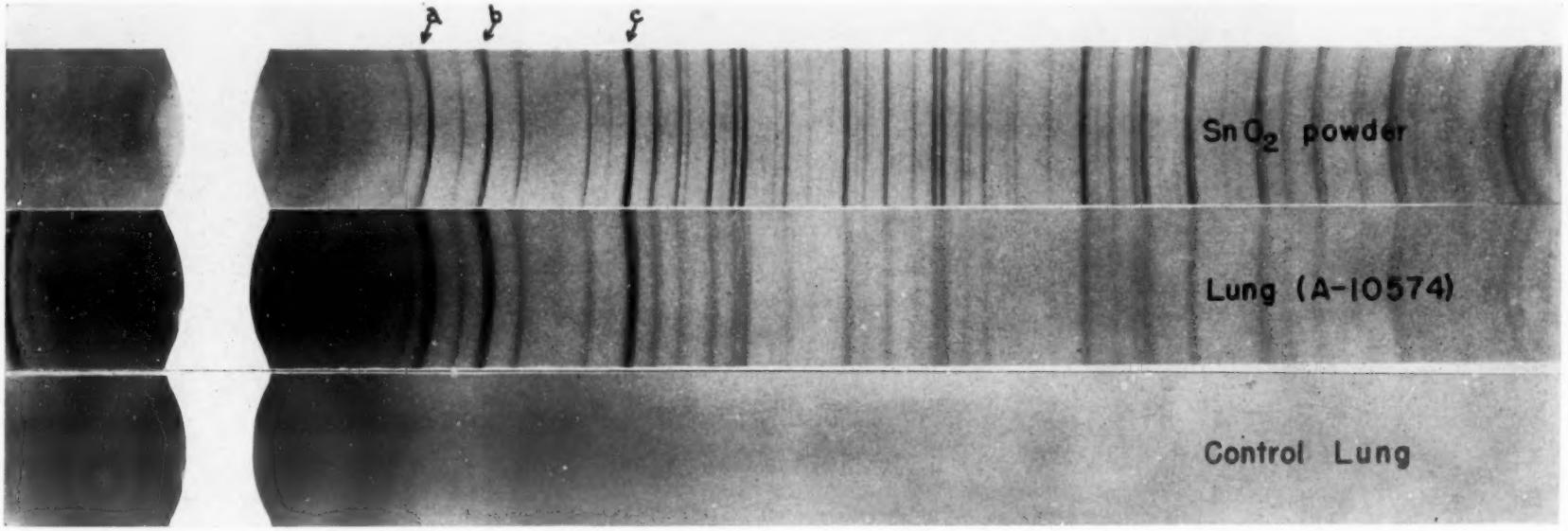

FIG. 10. Roentgen-ray diffraction patterns. All lines obtained with sample of stannotic lung are identical with those of SnO_2 powder. The interplanar spacings (*d* values) of the three strongest lines are: (*a*) 3.32 Å; (*b*) 2.60 Å; (*c*) 1.75 Å.

were readily dissolved by HCl alone, and were therefore considered to be compounds of calcium, iron or phosphorus. Crystalline particles present in the incinerated sections from a silicotic lung, on the other hand, withstood the action of not only HCl, but also of HCl and zinc.

Analytical Studies. Representative portions of parenchyma from each lung were weighed in the wet formalin-fixed state, dried at room temperature and reweighed, then ashed by incineration and weighed again. Since analytical results appear in the literature sometimes on the basis of wet tissue weight,[14] and sometimes as dry tissue weight,[20] values were calculated on both bases in this study.

Spectrographic Analysis. Samples of lung, liver, spleen, kidney, and bone were prepared for the spectrograph by the method outlined by Cholak and Story.[4] Suitable quantities of solutions of the ashed materials were placed in craters of purified graphite electrodes and the arc spectral region between 2,500 Å and 3,400 Å was photographed (Fig. 9). The lines were identified by comparison with the spectrum from an iron arc. For quantitative results a five step logarithmic sector was rotated before the slit of the spectrograph while the spectrum was photographed. The tin line at 2,840 Å and the lead line at 2,833 Å were chosen for measurement with a densitometer using internal standards for comparison. Samples of anthracotic lung tissue and of pure graphite were run as controls.

The concentrations of tin in the tissues are listed in Table I, and are compared with results obtained in a previous study in the same laboratory on the tissues of normal persons. The increased concentrations of tin noted in the liver and spleen may not be significant. The amount of tin in the lungs, however, was enormous, and in Table II is related to dry weight and ash content of the tissue. Identification of the specific compound of tin present, SnO_2, required roentgen-ray diffraction analysis as described below. The concentration of SnO_2 in the lungs was then calculated from its molecular weight. Because of the ready oxidation of volatilized tin, it is unlikely that any elemental particles of the metal were present.

Table I

CONCENTRATION OF TIN IN TISSUES

Tissue	Mg. of Tin per 100 gm. Wet Tissue	
	Detinner	Normal Human[14] (arithmetic mean values)
Lung	110.0	0.045
Liver	0.18	0.060
Spleen	0.64	0.022
Bone	0.01	0.050

Since no lines other than those of SnO_2 appeared on the diffraction pattern of the lung tissue, it can be said that SnO_2 was the only compound of tin present. In reference to the large SnO_2 content of the ash, 13.4 per cent, it may be recalled that microincineration of lung sections resulted in a white powdery ash, which is the characteristic form of SnO_2. The ash content of the dry lung tissue, 10.9 per cent, was more than twice the normal.

Lead concentrations in the tissues were within normal limits. Portions of lung tissue and lymph nodes were chemically analyzed for their silica content. The highest concentration of silica obtained in lung tissue was 98 milligrams per 100 grams dry tissue. This is slightly less than the 0.1 per cent silica content of dry tissue reported by Sweany[20] in normal persons. Analysis of bronchopulmonary lymph

Table II

ASH CONTENT OF LUNGS

	Per Cent Ash Content of Dry Tissue (gm. ash per 100 gm. tissue)	Per Cent Tin Content of Dry Tissue (gm. tin per 100 gm. tissue)		Ratio: SnO_2/Ash
		As Sn	As SnO_2	
Detinner	10.9	1.15	1.46	13.4%
Unexposed persons[14,20]	5.0	0.00045	—	—

nodes yielded 122 milligrams of silica per 100 grams of dry tissue.

Roentgen-Ray Diffraction Analysis. Representative portions of lung tissue were dried in vacuo at room temperature and pulverized in a mortar. Samples moistened with benzene were mounted in a "powder wedge" of the apparatus, a GE XRD-1 unit with accessory XRD powder camera. Employing a CA-6 Crystal Analysis Tube with copper target and a slit collimator with dimensions of 0.020 by 0.0125 inch, the exposure time was thirty minutes operating at 16 milliamperes and 40 kilovolts (peak). The diffraction pattern was recorded on strip film. Sharp lines were obtained. These lines compared precisely with those obtained from a sample of commercial SnO_2 powder (Tin Oxide White, Mallinckrodt) (Fig. 10). From the intervals at which the lines occurred on each of these films, as measured on a metric scale, the interplanar spacings ("d" values) were calculated by the application of Bragg's equation. The three strongest lines, by visual comparison, had spacings of 3.32 Å, 2.60 Å and 1.75 Å respectively. These values, as well as those for the weaker lines, agreed closely with those given for SnO_2 in the standard tables compiled by Hanawalt, Rinn and Frevel[10] for a large group of chemical substances. No other compounds, including those of tin, had listed spacings which compared so closely with those obtained from the subject lung. The spacing listed for the strongest line of silica (alpha-quartz) is 2.35 Å, but other lines of its diffraction pattern vary so greatly from those of SnO_2 that differentiation of the two compounds is unmistakable.

A sample of anthracotic lung from a routine autopsy was also prepared and a diffraction pattern obtained under duplicated conditions. No significant diffraction lines were obtained.

With a Geiger counter roentgen-ray spectrometer the mean crystallite dimension of SnO_2 in powdered lung tissue was determined to be 490 Å with a probable error range of from 440 Å to 560 Å. The smallest particles measured microscopically in the histologic preparations were of the order of 0.5 micron, or approximately ten times the mean dimension as determined by roentgen-ray diffraction. Thus, the particles observed by ordinary microscopy were polycrystalline aggregates, either inhaled in this form, or the result of agglomeration in the lungs.

DISCUSSION

Morphologic descriptions of the benign pneumoconioses are relatively rare in the literature. This undoubtedly is due to the fact that there are no gross or microscopic alterations which serve to differentiate these conditions from the very nearly ubiquitous anthracosis. People do not die because of the deposition of radiopaque particles in their lungs. In the absence of a chest roentgenogram or a history of exposure to a dust known to produce pneumoconiosis, the pathologist is not likely to undertake the analytical procedures necessary to demonstrate the true nature of the pneumoconiosis.

Gardner[9] recognized five general types of pneumoconiosis: (1) the clinically important forms, silicosis and asbestosis; (2) "modified silicosis," due to the inhalation of innocuous dusts, such as those of coal or iron, contaminated with free silica, and giving rise to appreciable degrees of pulmonary fibrosis; (3) those forms known chiefly from shadows cast on a roentgenogram, such as baritosis and the pseudonodulation of arc welders, usually symptomless, the roentgen-ray shadows thought to result from compact collections of radiopaque particles in the lungs without significant tissue reaction; (4) "benign nonspecific pneumoconiosis," such as simple anthracosis, provoking no significant fibrosis but merely pigmentation, and producing no roentgen-ray shadows, and (5) the group of reactions to organic dusts, inflammatory in nature, such as bagassosis. Inflammatory changes may also be caused by inorganic substances; the metals manganese, beryllium, vanadium and osmium give rise to a chemical pneumonitis.[18]

Pendergrass,[16,17] however, refers to the "roentgenologic conditions," baritosis, pseudonodulation of arc welders, and conditions seen in the lungs of certain metal grinders as "benign pneumoconiosis." To this group have been added those cases of roentgenographic reticulation due to the inhalation of finely divided particles of silver and iron oxide in silver polishers.[1]

McCord,[15], from a review of the literature, concludes that graphite dust may also lead to the development of a pneumoconiosis causing roentgen-ray shadows. These conditions are benign in the sense that they seldom produce symptoms other than cough in some cases, and that they have not been observed to cause significant pulmonary fibrosis, judging from the few autopsy cases recorded.[1,6]

Gardner[8] studied the action of numerous dusts, both siliceous and non-siliceous, in their capacity to irritate the tissues. Employing intravenous injection of saline suspensions of different mineral particles into animals, he classified them according to the type of tissue response produced. Free silica in various crystalline and amorphous forms provoked a nodular fibrosis which was often progressive. A large group of representative non-siliceous minerals, all of industrial importance as dusts, including anthracite and bituminous coal, produced simple phagocytosis, often with localized collections of lymphocytes, but no progressive tissue reaction. Various silicates produced an intermediate type of response. The dusts of the second group are spoken of as "inert" dusts, since their effect on tissue is minimal and clinically insignificant.

Gardner's choice of experiment,[8] the intravenous administration of dusts suspended in saline, is based on the assumption that a substance capable of initiating a tissue response would do so whether it be inhaled and deposited in the lungs, or whether it be widely distributed by the hematogenous route. He had shown that this was true of quartz particles, which, when injected intravenously, produced in the liver cellular injury and resultant whorled fibrous tissue foci identical with those found in the lungs in pulmonary silicosis. This method, however, does not reproduce the conditions of lymphatic blockage which prevail in the lungs following inhalation of massive quantities of a dust. Thus, dusts which provoke no tissue reaction when injected, and are therefore considered inert, result in microscopic degrees of pulmonary perilymphatic fibrosis when they are inhaled. It is proposed that this focal fibrosis is an effect of long-standing mechanical obstruction of the lymphatic channels. Every dust composed of particles of such size as to penetrate to the alveoli undergoes phagocytosis, and eventually clogs the lymphatics, produces a thickening of the surrounding areolar tissue which is due to a slight degree of fibrous tissue growth as well as to actual particle accumulation. A dust may be "inert" in that it is not toxic to cells, but no dust deposited in the lung in large quantity resides there without effect, however slight.

Study of the present case proves that stannic oxide may be included in the category of "inert" dusts, and justifies the designation of the pulmonary condition as a "benign pneumoconiosis," as suggested by Pendergrass[17] and others.[2,5] Its clinical benignity is indicated by the symptom-free interval of eighteen years following the final industrial dust exposure. At age seventy-two, vital capacity was still 85 per cent of normal. This moderate functional impairment was entirely consistent with the degree of chronic pulmonary emphysema present. The emphysema was of a nature to be expected in a man who had performed hard labor during a major portion of his productive years.

Although there was in all lobes slight thickening of the perivascular, peribronchial, pleural and interlobular septal lymphatic trunks due to marked foreign particle accumulation as well as to histiocytic proliferation and minimal fibrosis, the thickening was no greater than is commonly observed in cases of anthracosis. This degree of fibrosis was not sufficient to cast the shadows observed in the chest roentgenogram. These shadows had the pattern of, and were caused by, the compact accumulations of stannic oxide particles demonstrated in the microincinerated sections. Tin, of atomic weight 118.70, is a heavy metal. Pendergrass showed that stannic oxide powder is radiopaque, and when

introduced into the lungs of dogs by tracheal injection is capable of producing roentgen-ray shadows.[17]

The lower lobe of the left lung was the seat of organizing pneumonia with widespread plugging of alveoli by fibrin and often by fibrous tissue. The recent origin of this fibrous tissue was apparent in its rich cellularity. It was not evident on a roentgenogram made seven months before the patient's death, but appeared only as residual shadows following pneumonic involvement of the lobe. The adjacent bronchopulmonary lymph nodes were free of necrosis and focal fibrosis. The disease in this lobe cannot be directly attributed to pneumoconiosis. Pathologic fracture of a rib had occurred with consequent pneumothorax, probably by puncture of a pleural bleb. An acute pneumonia limited to this lobe was present four months later, and at autopsy a sharp bone edge was found embedded in the periphery of the lung. The irritating effect of the bone edge as an initiating factor in this infection and as a hindrance to resolution cannot be denied. Haythorn[11] is of the opinion that pulmonary anthracosis induces delayed resolution and organization of pneumonia because of retarded lymph flow. Choking of the lymphatic channels by stannic oxide dust as well as by carbon particles may have influenced the outcome of the pneumonia in the present case.

In sections from the upper lobe of the left lung there were occasional small arteries which had sclerotic changes in the intima. Small arteries in the left lower lobe were similarly affected, but more frequently and to a greater degree. Brenner, from an exhaustive study of pulmonary vascular lesions in a representative series of unselected autopsies concluded " . . . that sclerosis of the small muscular arteries is almost constant (though sometimes in only a few vessels) in patients over 40, irrespective of the presence or absence of chronic pulmonary or cardiac disease, but that . . . its severity . . . (is) somewhat greater in the presence of chronic cardiac or pulmonary disease, separately or together."[3] He found chronic pulmonary emphysema to be the most common pulmonary disease affecting the severity of the small artery sclerosis. The predominance of vascular change in the left lower lobe in the present case was probably related to the presence of long-standing organizing pneumonia, in addition to the pre-existing emphysema, and cannot be attributed specifically to the dust accumulation.

Enzer and Sander,[6] in their study of the only reported case of the pneumoconiosis of electric arc welders which had a postmortem examination, found stainable iron within clumps of carbon particles in the pulmonary lymphatics. Barrie and Harding[1] presented the intravitam staining of elastic tissue in the arterial and alveolar walls in their 4 cases of argyro-siderosis as an indication of the presence of inhaled silver dust. Carbon particles are easily recognized in tissue and are oxidized during incineration. No certain means of the identification of stannic oxide particles in tissue was known, however. Tin is so highly insoluble that a histologic stain cannot be applied. Nor have stannic oxide particles any identifying microscopic characteristics by ordinary illumination. By roentgen-ray diffraction analysis of dried tissue, silica was demonstrated in silicotic lungs by Sweany, Klaas and Clark.[19] This method was employed for the identification of the foreign particles in dried lung tissue in the present case. The tissue was not ashed for this purpose in order that the tin compound present would not be changed. The particle size fortunately was such that the diffraction lines were of good quality.

It may be significant that in 10 of the 11 reported cases of this condition, including the present one, the workers had either been furnace tenders, or had worked in the furnace room. Only 1 case[17] has been reported among the workers handling only the powdered finished product outside the furnace room, though this work is of a highly dusty nature. Cutter's 2 cases had each worked

at the detinning process for the same period of time, approximately twenty years. The man with the more marked roentgen changes operated the calcining furnace and was exposed chiefly to furnace fumes. Less pulmonary involvement was shown roentgenologically in the worker who performed chiefly the dustier work of grinding, sifting and packaging, though he also assisted in the operation of the furnace.[5] There is some volatilization of tin at the calcining temperatures (1,200° C.). Volatilized tin is rapidly oxidized, and the furnace fume consists largely of SnO_2. Considering the occupational histories of the reported cases, it is likely that exposure to furnace fumes rather than to dust from the finished product is the most important source of stannic oxide pneumoconiosis, a concept of significance in the control of the condition by industrial hygiene measures. A comparison might be made with the benign pneumoconiosis of arc welders, in which there is exposure to volatilized iron from electric arc welding.

Tin is one of the least toxic of the common metals when ingested in the form of its salts.[7,12] Man tolerates from 850 to 1,000 milligrams of free tin per day administered orally with meals. Kehoe[14] found the diet of a normal adult American to contain an average of 17.14 milligrams of tin per day, much of it derived from canned goods. It has been concluded, however, that there is little likelihood of chronic intoxication from this source. With relatively large doses of soluble salts of tin given intravenously, toxic changes have been produced in parenchymatous organs. Certain organic compounds of tin are considerably more toxic, but these are not of industrial importance. Acute industrial intoxication from exposure to tin has not occurred, and the rare cases of chronic poisoning reported are all of questionable validity. Stannic chloride is irritating to the skin, nose and eyes because of local hydrolysis, but this effect is not related to any toxic action of the metal. In none of the 10 previously reported cases of exposure to stannic oxide dust or fumes have there been clinical signs of heavy metal poisoning. Moreover, there was no anatomic evidence of damage to parenchymatous organs in the present case. While animals have not been subjected experimentally to the inhalation of stannic oxide, it must be concluded from the facts available on human exposures that the compound is of extremely low toxicity. Its marked insolubility undoubtedly is a factor, for after an interval of eighteen years during which he was free from exposure, the lungs of this man still contained enormous quantities of the compound. Systemic absorption of tin from the lungs following heavy exposure to SnO_2 by inhalation, occurs, if at all, to only an insignificant extent.

SUMMARY

A case of benign pneumoconiosis due to stannic oxide in a man aged seventy-two is presented with clinical, autopsy and analytical findings. An unusual chest roentgenogram consisting of uniform mottling of both lung fields by discrete, fine, dense shadows was encountered on a routine hospital admission film in 1948. There were no respiratory symptoms. Vital capacity was 85 per cent of normal. A history of exposure to dust and fumes from a detinning furnace for a period of eighteen years was obtained, this exposure having terminated in 1930.

The microscopic appearance of the lungs was that of moderate anthracosis. There was no necrosis nor nodular fibrosis of parenchyma or lymphoid tissue. On a roentgenogram of a thin lung slice there were dense perivascular, peribronchial and subpleural shadows. Examination of microincinerated sections under polarized light disclosed compact accumulations of bright yellowish-brown particles at these sites. The particles were soluble in HCl in the presence of powdered zinc and gave a positive spot test for tin. Spectrographic analysis disclosed abnormally large amounts of tin in the lungs. By roentgen-ray diffraction analysis of dried lung tissue

powder, a pattern identical with that of SnO_2 was obtained. The lungs contained 1.46 per cent SnO_2 dry weight, and the ash was composed of 13.4 per cent SnO_2. The silica content of lungs and lymph nodes was normal.

CONCLUSIONS

1. Inhalation of stannic oxide for long periods is productive of benign, symptomless pneumoconiosis with no significant pulmonary fibrosis.

2. Stannic oxide is radiopaque. Accumulation of particles in the regions of perivascular, peribronchial and subpleural lymphatics is productive of sharp shadows on the chest roentgenogram. These shadows are not cast by foci of fibrous tissue.

3. Tin deposited in the lungs in this form is non-toxic systemically.

4. Analytical and microincineration studies are necessary to differentiate this condition from simple anthracosis.

The authors are grateful to Drs. F. R. Dutra and K. Schmidt-Nielson of the Kettering Laboratory for their advice, to Messrs. J. Cholak, W. Younker and L. J. Schafer of Kettering Laboratory for the spectrographic and roentgen-ray diffraction studies, to Dr. J. W. Price of the Institute of Pathology, Western Reserve University, for the chemical determinations of tin and silica, and to Dr. L. E. Alexander of the Department of Research in Chemical Physics of the Mellon Institute of Industrial Research, University of Pittsburgh, for the roentgen-ray spectrometry. The photomicrographs were made by Mr. J. B. Homan of the Department of Medical Art of the College of Medicine, University of Cincinnati.

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REFERENCES

1. BARRIE, H. J., and HARDING, H. E. Argyrosiderosis of lungs in silver finishers. *Brit. J. Indust. Med.*, 1947, *4*, 225–229.
2. BARTAK, F., TOMECKA, M., and TOMICEK, O. Stannosis. *Casop. lék. cesk.*, 1948, *87*, 915–932.
3. BRENNER, O. Pathology of vessels of pulmonary circulation. *Arch. Int. Med.*, 1935, *56*, 457–497.
4. CHOLAK, J., and STORY, R. V. Spectrographic analysis of biological material. III. Lead, tin, aluminum, copper, and silver. *Indust. & Engin. Chem.* (Anal. Ed.), 1938, *10*, 619–622.
5. CUTTER, H. C., FALLER, W. W., STOCKLEN, J. B., and WILSON, W. L. Benign pneumoconiosis in tin oxide recovery plant. *J. Indust. Hyg. & Toxicol.*, 1949, *31*, 139–141.
6. ENZER, N., and SANDER, O. A. Chronic lung changes in electric arc welders. *J. Indust. Hyg. & Toxicol.*, 1938, *20*, 333–350.
7. FAIRHALL, L. T. Industrial Toxicology. Williams & Wilkins Company, Baltimore, 1949, pp. 176–178.
8. GARDNER, L. U. Etiology of pneumoconiosis. *J.A.M.A.*, 1938, *111*, 1925–1936.
9. GARDNER, L. U. Pathology and roentgenographic manifestations of pneumoconiosis. *J.A.M.A.*, 1940, *114*, 535–545.
10. HANAWALT, J. D., RINN, H. W., and FREVEL, L. K. Chemical analysis by x-ray diffraction. *Indust. & Engin. Chem.* (Anal. Ed.), 1938, *10*, 457–512.
11. HAYTHORN, S. R. Unresolved pneumonia associated with severe anthracosis. *Internat. A. M. Museums Bull.*, 1918, *7*, 49–52.
12. HEYROTH, F. F. The metals (except lead). In: Industrial Hygiene and Toxicology. Patty, F. A., Editor. Interscience Publishers, Inc., New York, 1949, Volume II, Chapter 22, pp. 730–732.
13. IRWIN, D. A. Histological demonstration of siliceous material by microincineration. *Canad. M.A.J.*, 1934, *31*, 135–140.
14. KEHOE, R. A., CHOLAK, J., and STORY, R. V. Spectrochemical study of normal ranges of concentration of certain trace metals in biological materials. *J. Nutrition*, 1940, *19*, 579–592.
15. MCCORD, C. P. Graphite (plumbago, black lead), as a source of dusty lung disease. *Indust. Med. & Surg.*, 1949, *18*, 483–486.
16. PENDERGRASS, E. P., and LEOPOLD, S. S. Benign pneumonoconiosis. *J.A.M.A.*, 1945, *127*, 701–795; addendum, 1945, *128*, 687.
17. PENDERGRASS, E. P., and PRYDE, A. W. Benign pneumoconiosis due to tin oxide. *J. Indust. Hyg. & Toxicol.*, 1948, *30*, 119–123.
18. PERRY, K. M. A. Diseases of lung from occupational dusts other than silica. *Thorax*, 1947, *2*, 91–120.
19. SWEANY, H. C., KLAAS, R., and CLARK, G. L. Detection of crystalline silica in lung tissue by x-ray diffraction analysis. *Radiology*, 1938, *31*, 299–307.
20. SWEANY, H. C., PORSCHE, J. D., and DOUGLASS, J. R. Chemical and pathologic studies of pneumonoconiosis, with special emphasis on silicosis and silicotuberculosis. *Arch. Path.*, 1936, *22*, 593–633.

Vol. 63, No. 6

ROENTGENOGRAPHIC CHANGES IN PULMONIC STENOSIS

A REPORT OF NINE CASES*

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PULMONIC stenosis associated with dextroposition of the aorta—the tetralogy of Fallot—is a relatively common congenital anomaly. Pure pulmonic stenosis, however, has been considered a rare malformation. Inasmuch as 8 cases of uncomplicated pulmonic stenosis have been diagnosed by venous catheterization of the heart during the last few years at this hospital, it would appear that a more careful search for the existence of this anomaly will uncover an increasing number of cases. It is the purpose of this paper to describe the roentgenographic appearance of mild pulmonic stenosis as illustrated by these 8 cases. One case of severe pulmonic stenosis, complicated by a small right-to-left shunt through a septal defect, will also be discussed.

METHODS

Eight cases of uncomplicated pulmonic stenosis and one with an associated septal defect were subjected to venous catheterization of the heart and pulmonary artery.[4,5] Pressures in the cardiac chambers and in the pulmonary artery were recorded by a Hamilton manometer.[10] Cardiac output was calculated by the Fick principle.[5] The degree of pulmonic stenosis was estimated by calculating the resistance to blood flow offered by the stenosis as described elsewhere.[7]

The diagnosis of pulmonic stenosis was based on criteria set forth in an earlier report.[7] A higher systolic pressure in the body of the right ventricle than in its outflow tract or in the pulmonary artery established the presence of a stenosis between the high and low pressure areas. Physiologically significant septal defects were excluded by blood sampling from the pulmonary artery, right heart chambers, and the superior vena cava and by the absence of arterial oxygen unsaturation in all but Case III. The identity of right ventricular and systemic arterial systolic pressures, which is physiologic evidence of an overriding aorta,[6] was not present in any of these patients.

Heart size was measured by the method of Ungerleider and Clark.[17] Changes in the size of the "main pulmonary artery" were recorded. The term "main pulmonary artery" refers to a localized convexity on the left heart border seen immediately beneath the aortic knob in the posteroanterior projection. Actually this convexity is made up of the main pulmonary artery and the proximal portion of its left main branch.[2] Changes in the size of the hilar and intrapulmonary branches were also separately recorded. To facilitate the interpretation of these changes, a system of grading them from -1 to $++++$ was established. This grading scale has been illustrated in detail in a previous paper.[11] A similar scale was employed for describing selective cardiac chamber enlargement as observed in the posteroanterior and both oblique projections. Finally, hyperactivity or expansile pulsations of the pulmonary artery, noted at roentgenoscopy, were recorded as $+$ if moderate and $++$ if marked in extent.

Because there is no pediatric service in this hospital, all patients were over the age of eleven. This report describes, therefore, the roentgenographic appearance of pulmonic stenosis which has permitted life beyond at least the age of eleven.

* This work was supported in part by a grant from the Life Insurance Medical Research Fund.

OBSERVATIONS

Table I summarizes the altered hemodynamics and the structural changes recognizable by routine roentgenographic methods in 9 cases of pulmonic stenosis. Of these 9 cases, only 1 (Case III) could be classified as a severe pulmonic stenosis. This case had an extreme elevation of right ventricular pressure, a low cardiac output, and a small right-to-left shunt either through a ventricular or auricular septal defect. The obstruction in this case, as may be seen from the high stenosis resistance, was extreme. The remaining 8 cases had mild pulmonic stenosis as judged by the stenosis resistances.[7] Right ventricular pressures were either slightly or moderately elevated. Their calculated outputs, except for Case IX, were normal. The calculated output in Case IX was thought to be falsely low. In none of them was there a detectable shunt across a septal defect.

Demonstrable cardiac enlargement was present in only 2 of the 9 cases. Evidence of right ventricular enlargement was seen in the left anterior oblique position in 3 cases, but in none of the remaining cases. In only 1 case did the right auricle appear unusually prominent. Despite the fact that in 2 cases (Cases III and VII) the left ventricle appeared large, the electrocardiogram showed definite evidence of right ventricular hypertrophy only. Left auricular enlargement was not observed in any of the cases.

Six of the cases showed definite enlargement of the "main pulmonary artery" and in 5 of these there was definite hyperactivity of that structure. In none of the cases was there an increase in the size or activity of the hilar or peripheral branches of the pulmonary artery.

TABLE I

ROENTGENOGRAPHIC CHANGES, BLOOD FLOWS, AND PRESSURES IN 9 CASES OF PULMONIC STENOSIS

Number	Name	Main Pulmonary Artery		Hilar Branches		Intrapulmonary Branches—Size	Heart Size	Chamber Size				Pressures mm. Hg		Cardiac Index—l/min/sq.m.	Pulmonic Stenosis Resistance Dyne sec. cm.$^{-5}$ (ref. 7)
		Size	Activity	Size	Activity			Right Ventricle	Left Ventricle	Right Auricle	Left Auricle	Main Right Ventricle	Pulmonary Artery		
1	A.J.	+++	+	N	N	N	N	N	N	N	N	80/8	16/8	2.9	656
2	W.H.	+++	+	N	N	N	N	N	N	N	N	34/2	23/15	3.5	69
†3	J.T.	+++	+	N	N	—	+30%	++	+	++	N	151/0	26/9	2.0	2880
4	W.P.	++	++	N	N	N	N	N	N	N+	N	39/4	23/6	4.6	99
5	D.S.	++	+	N	N	N	N	N	N	N	N	83/3	20/13	3.4	357
6	T.M.	++	N	N	N	N	N	N	N	N	N	40/2	26/5	3.1	186
7	R.L.	N+	N	N	N	N	+25%	++	+	+	N	99/2	33/14	3.6	498
8	E.R.	N	N	N	N	N	N	N	N	N+	N	35/6	22/15	3.4	106
*9	J.M.	N	N	N	N	N	N	N	N	N+	N	85/0	28/10	1.8	284

N = Normal.
N+ = Prominent but not exceeding outside range of normal.
* Calculated cardiac index thought to be falsely low.
† This patient had a small right-to-left shunt (0.6 l/min.) unaffected by breathing 100 per cent oxygen.

DISCUSSION

The circulatory changes consequent to pulmonic stenosis have been described in detail elsewhere.[7] The principal effect of pulmonic stenosis is to increase the work of the right ventricle which must function against a resistance even in the resting state. Increased work leads to hypertrophy of this chamber. Right auricular work is not increased unless right auricular pressure rises. Since the left auricle and the left ventricle are beyond the stenosis, they per-

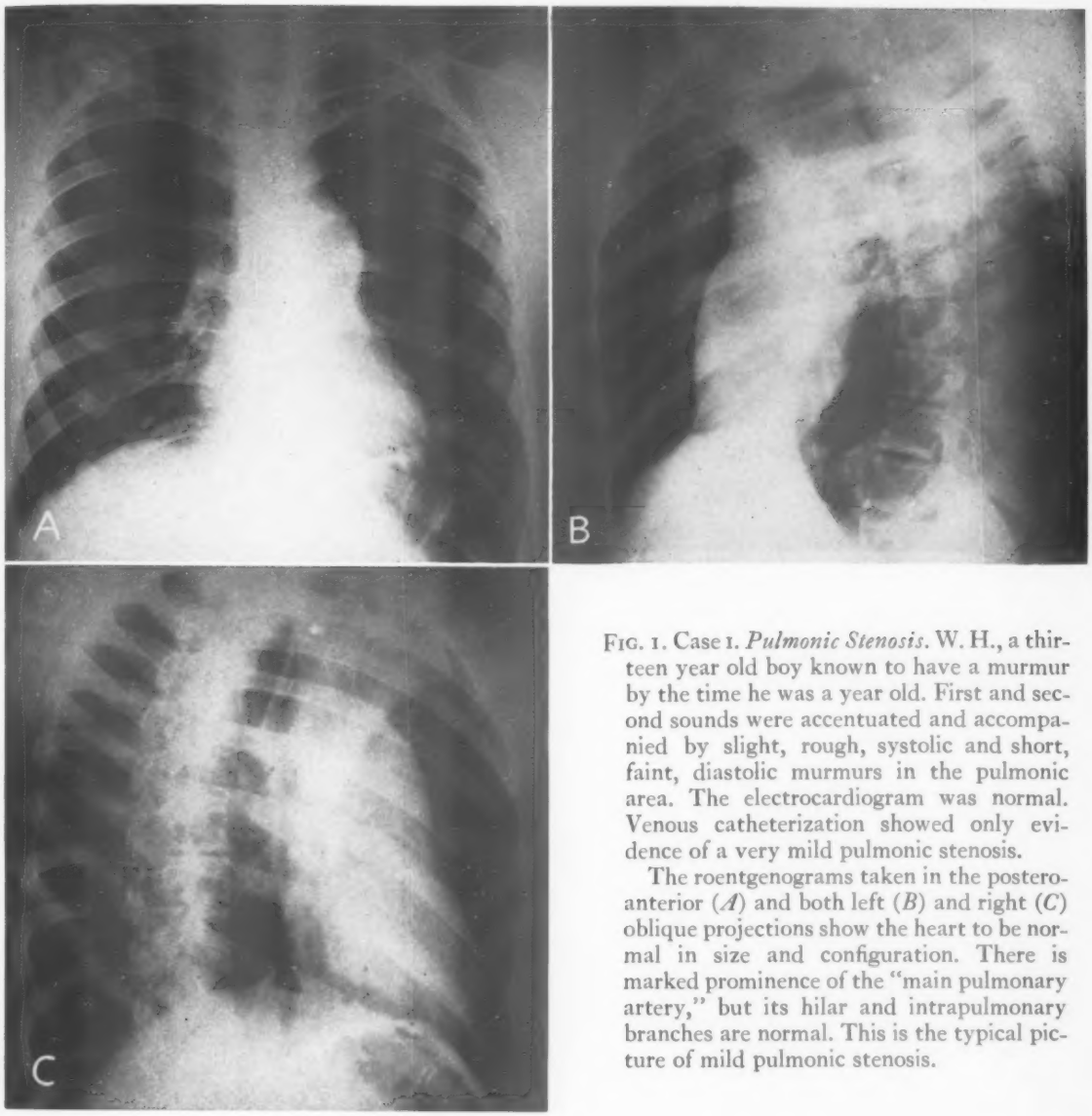

Fig. 1. Case 1. *Pulmonic Stenosis.* W. H., a thirteen year old boy known to have a murmur by the time he was a year old. First and second sounds were accentuated and accompanied by slight, rough, systolic and short, faint, diastolic murmurs in the pulmonic area. The electrocardiogram was normal. Venous catheterization showed only evidence of a very mild pulmonic stenosis.

The roentgenograms taken in the postero-anterior (*A*) and both left (*B*) and right (*C*) oblique projections show the heart to be normal in size and configuration. There is marked prominence of the "main pulmonary artery," but its hilar and intrapulmonary branches are normal. This is the typical picture of mild pulmonic stenosis.

form no unusual work and need not hypertrophy. The pulmonary artery distal to the stenosis transmits either a normal or reduced amount of blood at normal or slightly reduced pressures in the resting state. It is therefore subjected to no unusual distending force.

The anatomical changes of pulmonic stenosis are well known and have been recently described in several review articles. The stenosis may occur either at the pulmonary valve or just proximal to it in the infundibulum or the right ventricle.[16] Greene *et al.*[9] reviewed 68 cases of pulmonic stenosis confirmed at autopsy and found definite mention of right ventricular hypertrophy in all but 6 of the cases. In 8 of the 11 cases reported by Currens, Kinney and White,[3] there was definite enlargement of the right atrium. Dexter's group was unable to find a description of left atrial or left ventricular enlargement unless additional causes for enlargement of the left side of the heart were present.[7] A post-stenotic dilatation of the pulmonary artery was present in 33 of the 68 cases reviewed

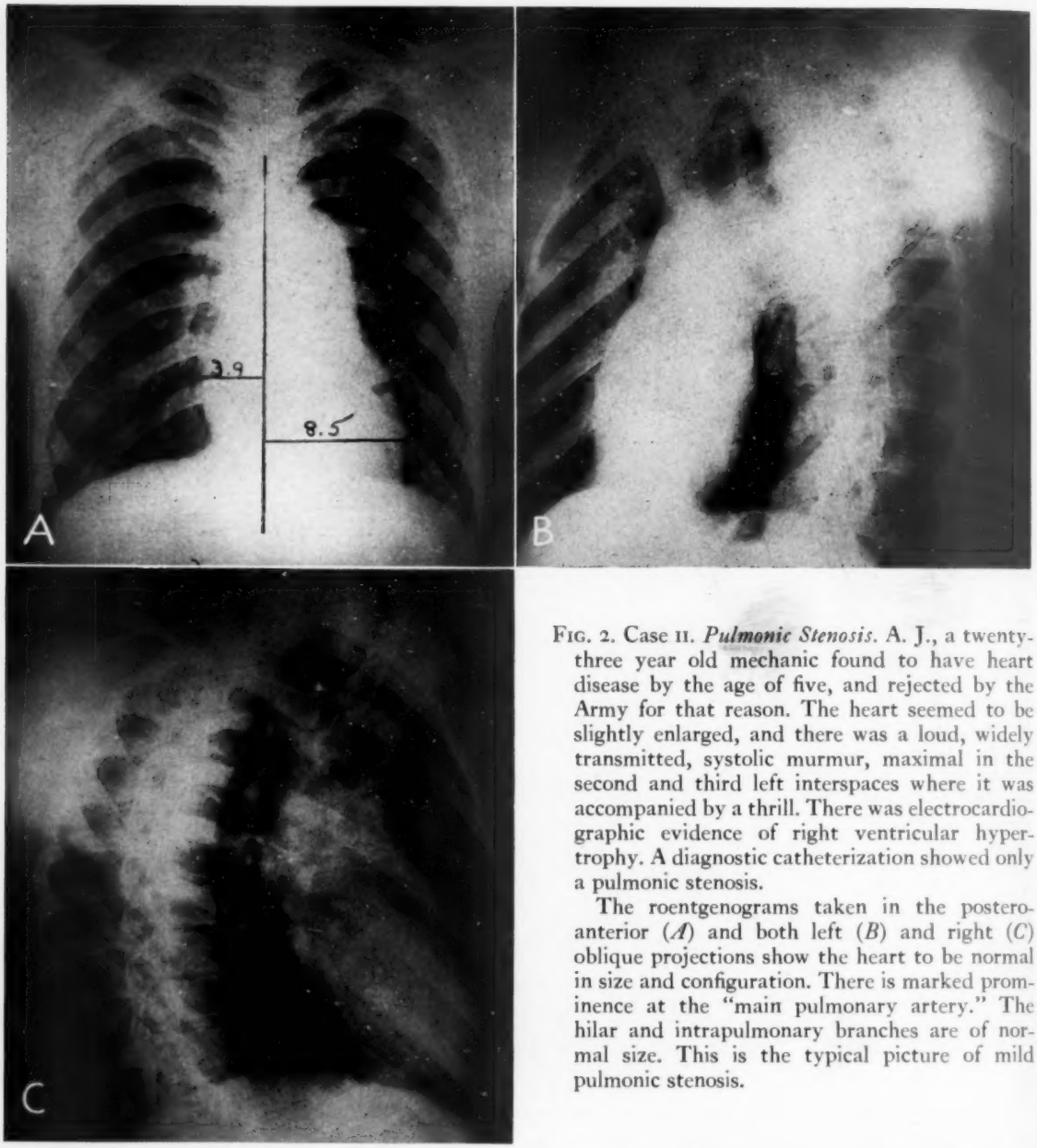

FIG. 2. Case 11. *Pulmonic Stenosis.* A. J., a twenty-three year old mechanic found to have heart disease by the age of five, and rejected by the Army for that reason. The heart seemed to be slightly enlarged, and there was a loud, widely transmitted, systolic murmur, maximal in the second and third left interspaces where it was accompanied by a thrill. There was electrocardiographic evidence of right ventricular hypertrophy. A diagnostic catheterization showed only a pulmonic stenosis.

The roentgenograms taken in the postero-anterior (*A*) and both left (*B*) and right (*C*) oblique projections show the heart to be normal in size and configuration. There is marked prominence at the "main pulmonary artery." The hilar and intrapulmonary branches are of normal size. This is the typical picture of mild pulmonic stenosis.

by Greene. Selzer *et al.*[14] made a similar observation in their review. Many explanations have been advanced for this post-stenotic dilatation of the pulmonary artery in pulmonic stenosis,[7,13] but at present no indisputable anatomical or physiological explanation is known. The other anatomical changes described above are perfectly consistent with the altered hemodynamics of this condition.

The roentgenographic appearance of pulmonic stenosis has been repeatedly described.[1,3,8,9,12,13,14,15,16] These descriptions, largely based on cases proved at autopsy, have emphasized enlargement of the right atrium and ventricle and frequently localized enlargement of the main pulmonary artery. Roesler[13] has pointed out the diagnostic importance of the localized enlargement of the main pulmonary artery in pulmonic stenosis. Recently Selzer *et al.*[14] have noted that this enlargement of the

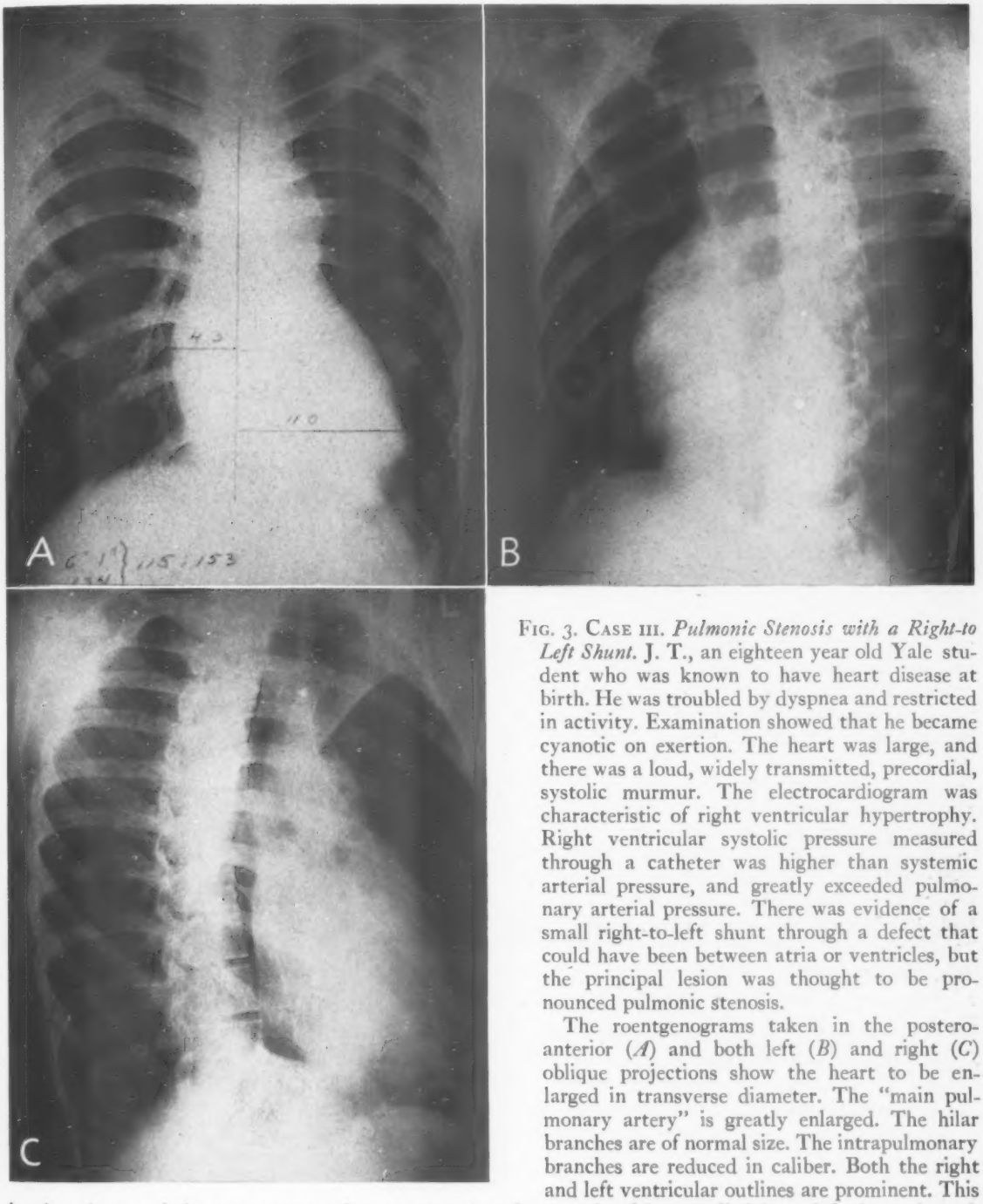

FIG. 3. CASE III. *Pulmonic Stenosis with a Right-to Left Shunt.* J. T., an eighteen year old Yale student who was known to have heart disease at birth. He was troubled by dyspnea and restricted in activity. Examination showed that he became cyanotic on exertion. The heart was large, and there was a loud, widely transmitted, precordial, systolic murmur. The electrocardiogram was characteristic of right ventricular hypertrophy. Right ventricular systolic pressure measured through a catheter was higher than systemic arterial pressure, and greatly exceeded pulmonary arterial pressure. There was evidence of a small right-to-left shunt through a defect that could have been between atria or ventricles, but the principal lesion was thought to be pronounced pulmonic stenosis.

The roentgenograms taken in the postero-anterior (*A*) and both left (*B*) and right (*C*) oblique projections show the heart to be enlarged in transverse diameter. The "main pulmonary artery" is greatly enlarged. The hilar branches are of normal size. The intrapulmonary branches are reduced in caliber. Both the right and left ventricular outlines are prominent. This is the characteristic appearance of a severe pulmonic stenosis with a small right-to-left shunt through a septal defect.

main pulmonary artery may also extend into the proximal portion of the left main branch, but that the peripheral branches remain undilated.

It is evident from Table 1 that mild pulmonic stenosis would be unsuspected in the majority of the cases if its recognition depended on roentgenographic evidence of cardiac or chamber enlargement (see Fig. 1, 2 and 4). Actually only 3 cases showed

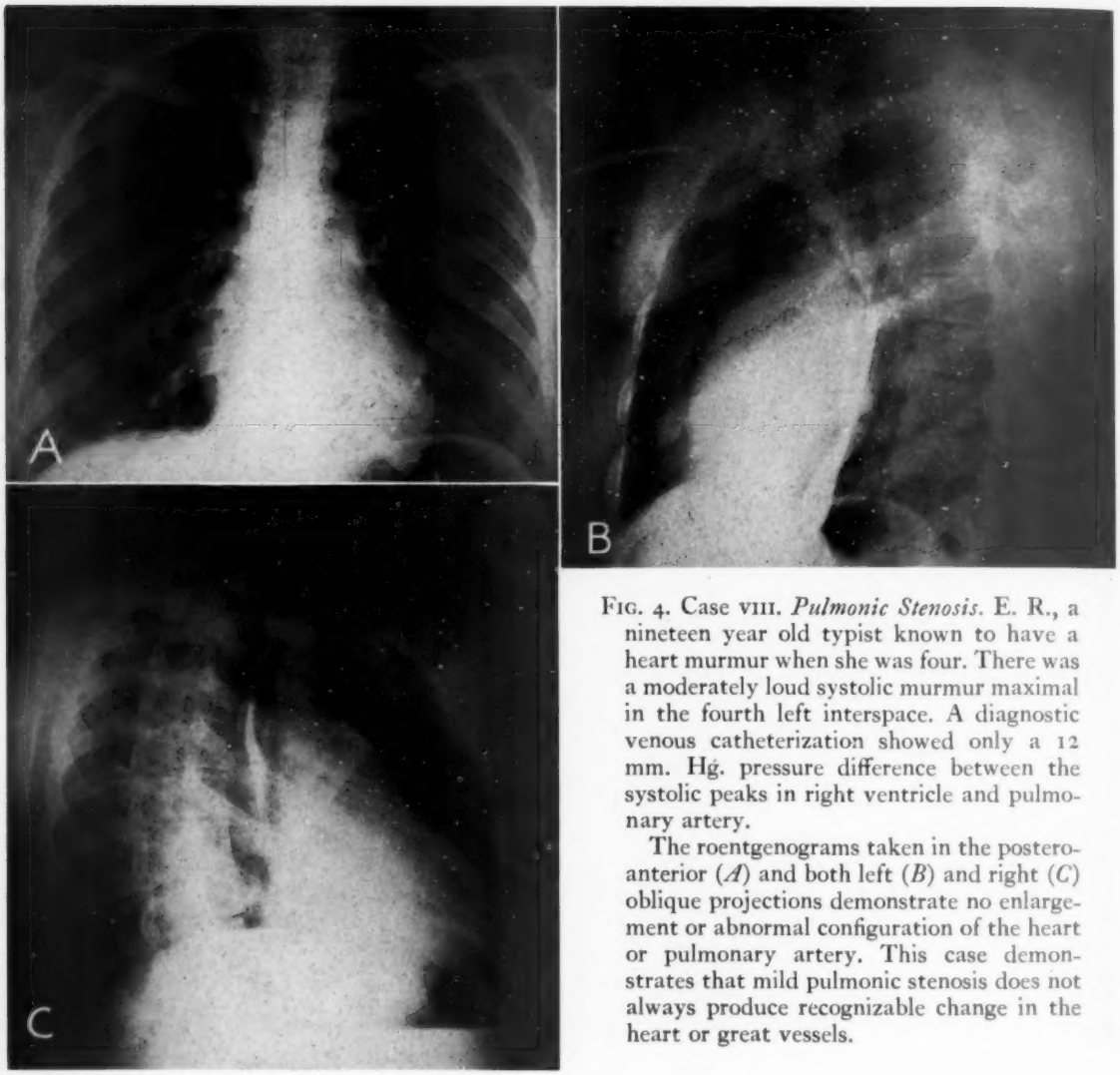

FIG. 4. Case VIII. *Pulmonic Stenosis.* E. R., a nineteen year old typist known to have a heart murmur when she was four. There was a moderately loud systolic murmur maximal in the fourth left interspace. A diagnostic venous catheterization showed only a 12 mm. Hg. pressure difference between the systolic peaks in right ventricle and pulmonary artery.

The roentgenograms taken in the posteroanterior (*A*) and both left (*B*) and right (*C*) oblique projections demonstrate no enlargement or abnormal configuration of the heart or pulmonary artery. This case demonstrates that mild pulmonic stenosis does not always produce recognizable change in the heart or great vessels.

any recognizable abnormality in cardiac size or right heart configuration (Fig. 3). Moreover, in 2 of these 3 cases, right ventricular enlargement simulated left ventricular enlargement on the roentgenogram —a finding incompatible with the diagnosis of isolated pulmonic stenosis. The absence of demonstrable left atrial enlargement is valuable negative evidence in that an enlarged left atrium would exclude the diagnosis of uncomplicated pulmonic stenosis.

In contrast to the minimal changes in the cardiac chambers, the pulmonary artery showed a definite change in 6 of the 9 cases. This change was characterized by a definite enlargement and hyperactivity of the "main pulmonary artery" without an associated enlargement or hyperactivity of its hilar or intrapulmonary branches (Fig. 1, 2 and 3).

In a certain number of cases, mild pulmonic stenosis may be present without producing any recognizable changes on roentgenographic examination. Figure 4 illustrates such a case.

DIFFERENTIAL DIAGNOSIS

Inasmuch as the roentgenographic changes of mild pulmonic stenosis are best recognized by noting a prominent pul-

monary artery when present, it is only necessary to consider in differential diagnosis those conditions which produce changes in the pulmonary artery that might be confused with pulmonic stenosis.

In a previous paper it was pointed out that an abnormal increase in resting blood flow or pressure in the pulmonary artery will produce an enlargement and hyperactivity of the "main pulmonary artery" which is quite comparable to that seen in pulmonic stenosis. It was emphasized, however, that in cases of increased resting flow or pressure, unlike pulmonic stenosis, this enlargement extends to include the hilar and intrapulmonary branches. Pulmonic stenosis may therefore be distinguished from atrial septal defect, ventricular septal defect, patency of the ductus arteriosus, Eisenmenger's complex, mitral stenosis and from primary or secondary pulmonary arteriolar obstruction with cor pulmonale, for in each of these conditions enlargment of the main pulmonary artery and its branches results from an increased resting pulmonary arterial flow or pressure.[11]

This differential point is not an absolute one, for out of a total of 33 cases that had an enlarged main pulmonary artery result-

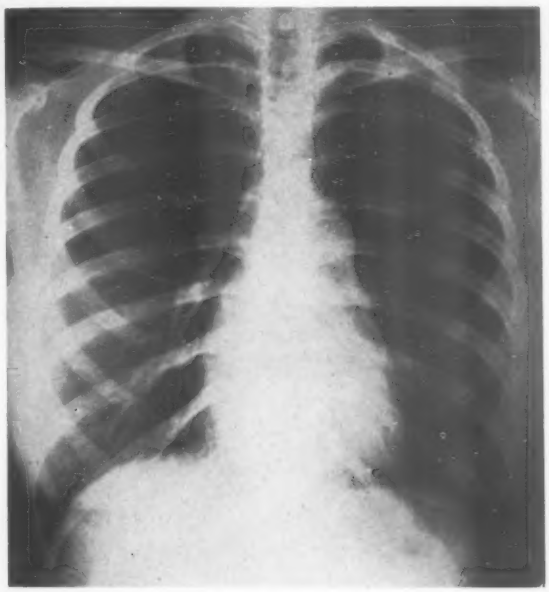

Fig. 5. *Strial Septal Defect.* B. K., a nineteen year old, married girl who had been excessively restricted because of a murmur heard at the age of five years. There was a loud, rough, systolic murmur and thrill, maximal in the pulmonic area. The electrocardiogram showed right bundle branch block. A venous catheterization showed a large shunt from left to right atrium. There was a 4 to 7 mm. Hg. pressure difference between systolic peaks in right ventricle and pulmonary artery. This discrepancy in pressures was considered inadequate to support an additional diagnosis of pulmonic stenosis.

The roentgenogram shows the main pulmonary artery to be prominent. The hilar and intrapulmonary branches are within the limits of normal in size. This case was thought to be a pulmonic stenosis prior to catheterization. Despite this exception, the difference between an atrial septal defect and pulmonic stenosis is usually readily seen on routine roentgenograms.

Fig. 6. *Pulmonary Vascular Disease.* M. Q., a thirty-two year old woman who became subject to attacks of syncope two and a half years before study. Exertional dyspnea was noted one year later, and finally ankle edema. There was only a faint, precordial, systolic murmur. Right ventricular hypertrophy was apparent by electrocardiogram. Venous catheterization demonstrated a high resistance to flow through the lung with elevated pulmonary arterial pressure and reduced cardiac output. At postmortem examination an obliterative arteriosclerosis of the pulmonary vasculature was found.

The roentgenogram shows marked cardiac enlargement. The striking prominence of the main pulmonary artery in the presence of normal hilar and intrapulmonary branches simulates pulmonic stenosis. None was present on catheterization. It should be emphasized however that it is unusual for cor pulmonale to resemble pulmonic stenosis.

FIG. 7. *Tetralogy of Fallot.* S. K., a nine year old girl who developed bacterial endocarditis with pulmonary emboli. There was slight digital clubbing and cyanosis. A widely transmitted precordial systolic murmur and thrill were present. The electrocardiogram showed marked right ventricular hypertrophy. Cardiac catheterization revealed a severe pulmonic stenosis with low pulmonary arterial pressure and a reduced pulmonary blood flow. A small right-to-left shunt was present.

The roentgenogram shows marked cardiac enlargement. The main pulmonary artery is greatly dilated but the hilar and intrapulmonary branches are reduced in caliber.

ing from either increased pressure or flow, 2 cases failed to show the expected enlargement of the hilar and intrapulmonary branches.[11] One of these, illustrated in Figure 5, was diagnosed on roentgenographic examination as pulmonic stenosis, but proved to be an atrial septal defect with a moderately increased pulmonary arterial flow. The second exception, illustrated in Figure 6, also resembling pulmonic stenosis, was found on cardiac catheterization to have a markedly elevated pulmonary arterial pressure as a consequence of a high degree of pulmonary arteriolar obstruction. An autopsy on this case revealed advanced pulmonary arteriolar disease without any evidence of pulmonic stenosis.

Despite the existence of exceptions, the appearance of the main pulmonary artery and its branches remains the most important roentgenographic differential point between pulmonic stenosis and the conditions listed above. Left auricular enlargement, when present in mitral stenosis and patency of the ductus arteriosus or in interventricular septal defect, will exclude the diagnosis of simple pulmonic stenosis. Roentgenographic evidence of left ventricular enlargement may be used to exclude pulmonic stenosis with certainty only if it is verified by electrocardiographic findings.

The "main pulmonary artery" in the tetralogy of Fallot is usually either normal or reduced in size. In the unusual case, however, the pulmonary artery in the tetralogy may duplicate exactly the changes of pulmonic stenosis. Such a case is illustrated in Figure 7.

Finally, there is the unusual case with normal hemodynamics on cardiac catheterization which presents a dilated "main pulmonary artery" which is indistinguishable by roentgenographic methods from pulmonic stenosis. The similarity of these two conditions is apparent from Figure 8.

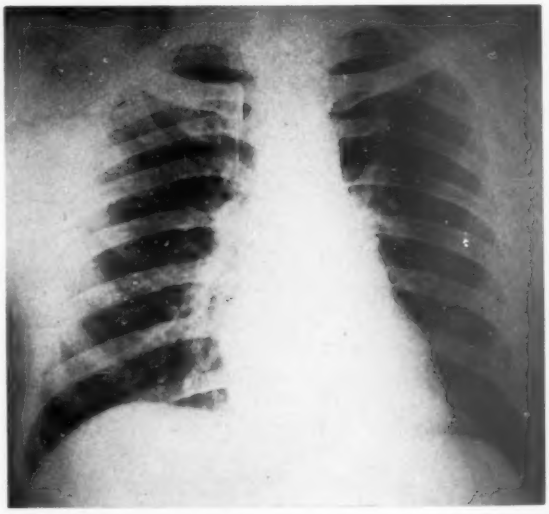

FIG. 8. *Dilated Main Pulmonary Artery with Normal Hemodynamics.* L. F., a much concerned, thirty-five year old man, who was found to have an enlarged pulmonary artery by roentgenoscopy. There was only a faint, variable, pulmonic, systolic murmur. The electrocardiogram was normal, as were the findings of a diagnostic catheterization.

On the original roentgenogram there was definite enlargement of the main pulmonary artery with normal-sized hilar and intrapulmonary branches. The reason for the dilated "main pulmonary artery" in this case remains obscure.

SUMMARY

An analysis has been made of the roentgenographic and hemodynamic changes observed in eight cases of mild uncomplicated pulmonic stenosis and in one case of severe pulmonic stenosis complicated by a right-to-left shunt through a septal defect but without an overriding aorta.

The most significant roentgenographic finding in six of these nine cases was a poststenotic dilatation of the "main pulmonary artery" which did not extend to include the hilar or intrapulmonary branches. This finding has been observed by others.

The majority of cases failed to show cardiac or selective chamber enlargement. Left auricular enlargement was not observed in any of the cases.

A differential diagnosis of pulmonic stenosis based on the appearance of the pulmonary artery and the absence of left auricular enlargement was given. Included in the differential were atrial septal defect, ventricular septal defect, patency of the ductus arteriosus, Eisenmenger's complex, mitral stenosis, cor pulmonale, the tetralogy of Fallot, and a dilatation of the pulmonary artery from unknown cause.

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REFERENCES

1. Bedford, D. E., Papp, C., and Parkinson, J. Atrial septal defect. *Brit. Heart J.*, 1941, *3*, 37–68.
2. Chavez, I., Dorbecker, N., and Celis, A. Direct intracardiac angiocardiography; its diagnostic value. *Am. Heart J.*, 1947, *33*, 560–593.
3. Currens, J. H., Kinney, T. D., and White, P. D. Pulmonary stenosis with intact interventricular septum. *Am. Heart J.*, 1945, *30*, 491–510.
4. Dexter, L., and others. Studies of congenital heart disease; technique of venous catheterization as a diagnostic procedure. *J. Clin. Investigation*, 1947, *26*, 547–553.
5. Dexter, L., and others. Studies of congenital heart disease; pressure and oxygen content of blood in right auricle, right ventricle, and pulmonary artery in control patients, with observations on the oxygen saturation and source of pulmonary "capillary" blood. *J. Clin. Investigation*, 1947, *26*, 554–560.
6. Dexter, L. Unpublished observations.
7. Dow, J. W., and others. Studies of congenital heart disease. IV. Uncomplicated pulmonic stenosis. *Circulation*, 1950, *1*, 267–287.
8. Eakin, W. W., and Abbott, M. E. Stenosis of pulmonary conus at lower bulbar orifice (conus a separate chamber) and closed interventricular septum, with 2 illustrative cases. *Am. J. M. Sc.*, 1933, *186*, 860–870.
9. Greene, D. G., Baldwin, E. deF., Baldwin, J. S., Himmelstein, A., Roh, C. E., and Cournand, A. Pure congenital pulmonary stenosis and idiopathic congenital dilation of the pulmonary artery. *Am. J. Med.*, 1949, *6*, 24.
10. Hamilton, W. F., Brewer, G., and Brotman, I. Pressure pulse contours in the intact animal; analytical description of a new high-frequency hypodermic manometer with illustrative curves of simultaneous arterial and intracardiac pressures. *Am. J. Physiol.*, 1934, *107*, 427–435.
11. Healey, R. F., Dow, J. W., Sosman, M. C., and Dexter, L. Relationship of roentgenographic appearance of pulmonary artery to pulmonary hemodynamics. Am. J. Roentgenol. & Rad. Therapy. 1949, *62*, 777–787.
12. Lowance, M. I., Jones, E. C., Mathews, W. B., and Dunstan, E. M. Congenital pulmonary stenosis. *Am. Heart J.*, 1948, *35*, 820–824.
13. Roesler, H. Clinical Roentgenology of the Cardiovascular System: Anatomy, Physiology, Pathology, Experiments and Clinical Applications. Charles C Thomas, Springfield, Illinois, 1937.
14. Selzer, A., Carnes, W. H., Noble, C. A., Higgins, W. H., and Holmes, R. O. Syndrome of pulmonary stenosis with patent foramen ovale. *Am. J. Med.*, 1949, *6*, 3.
15. Stauffer, H. M. Roentgenology of congenital heart disease. *Bull. U. Minn. & Minn. Med. Found.*, 1948, *19*, 486.
16. Taussig, Helen B. Congenital Malformations of the Heart. The Commonwealth Fund, New York, 1947.
17. Ungerleider, H. E., and Clark, C. P. Study of transverse diameter of heart silhouette with prediction table based on teleoroentgenogram. *Am. Heart J.*, 1939, *17*, 92–102.

TUBERCULOMA OF THE DIAPHRAGM*

REPORT OF ONE CASE

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THE purpose of this paper is two-fold: first, to present the roentgenological manifestation of a pathological rarity and second, to illustrate the importance of roentgenological examination in its early diagnosis. Up to 1941,† only 16 instances of benign or malignant primary growth of the diaphragm had been recorded in the literature. Of the 6 cases reported previous to 1930, the diagnosis was made either on necropsy or at such a late stage of the disease that involvement of the chest wall with external bulging had already taken place. It is interesting to note that in the next decade more cases appeared in the literature, and some of them were diagnosed at a comparatively early stage of the disease. This advancement is early diagnosis was accomplished mainly through improvement of the roentgenological method of investigation of chest diseases. A localized diaphragmatic growth can be clearly demonstrated on roentgen examination in almost every case, and usually there is scarcely any difficulty in its detection. In Ballon and Spector's case, however, the lesion, which was situated on the left side and overshadowed by the heart, was entirely overlooked before the postmortem examination. This illustrates the importance of complete roentgenological study, including, if necessary, examination with pneumothorax, pneumoperitoneum and kymography.

Although the present case is concerned with an inflammatory lesion, yet, as judged by the gross appearance of the mass, especially from the roentgenological point of view, it may well be considered together with diaphragmatic tumors. Inasmuch as no roentgenological study of such a pathological condition has ever been reported in the past, a brief review of the present case, particularly with reference to the differential diagnosis and preoperative determination of the size, shape and exact location of the mass, seems to be justified. The cases of diaphragmatic tumors reported previously are summarized in Table 1 for comparison.

CASE REPORT

A Chinese male, aged twenty-four, was referred for roentgenological examination of the chest on December 4, 1940, because of pain in the right lower chest of one month's duration. The patient had been an employee in the hospital since July, 1939. The routine physical examination at the time of employment, including urine, stool and blood Wassermann test as well as roentgen examination of the chest (Fig. 1), gave normal findings. Onset of the present illness was insidious and the pain was never bad enough as to prevent him from attending to his duty. There was some cough and slight loss of body weight; otherwise, his general health was good. The past history revealed nothing remarkable. The roentgenological findings of the chest on December 4, 1940 were recorded as follows (Fig. 2, 3 and 4):

"The left lung appears normal. On the right side the lung field is essentially clear. The interlobar pleura is visible. There is a round, localized bulging at the medial portion of the hemidiaphragm. In the lateral view, it appears quite anteriorly situated. The diaphragmatic movement is less on this side, particularly in the region of the bulging. This is confirmed by kymographic study. Mild pleural thickening is present in the costophrenic region."

* From the Department of Radiology, Peiping Union Medical College, Peiping, China.
† Literature since December, 1941, is not available for review to bring the study up to date.

TABLE I

TABLE SHOWING CASES OF DIAPHRAGMATIC TUMORS

Author	Sex and Age of Patient	Type and Location of Tumor	Diagnostic Procedure	Remarks
Clark (1887)	F 65	Lipoma (right)	Autopsy	No sign
Dalzell (1887)	F 42	Round cell sarcoma (right)	Autopsy	No symptom or sign
Gross (1911)	M 30	Fibrosarcoma (left)	Operation	Mass under left costal margin. Pleuritic pain
Bonamy (1912)	F 34	Multiple myofibroma (right)	Operation	Swelling of right side of chest
Sauerbruch (1913)	F 43	Fibromyosarcoma (left)	Operation	Mass palpable in left hypochondrium
Van Nes (1921)	M 65	Fibrosarcoma (left)	Autopsy	Chest pain, dyspnea and cyanosis
Burvill-Holmes and Brody (1932)	M 50	Angiofibroma (right)	Roentgen ray and autopsy	Accidental roentgen discovery in a case of bilateral pulmonary tuberculosis
Müller (1933)	F 45	Myoblastic sarcoma (right)	Autopsy	
Kirshbaum (1935)	M 47	Rhabdomyosarcoma (right)	Autopsy (negative roentgen findings)	Cough, hemoptysis, pain in left chest and weight loss. Metastases in both lungs
Kirshbaum (1935)	M 58	Leiomyosarcoma (left)	Autopsy (negative roentgen findings)	Mass in left upper quadrant
Söderlund (1937)	F 50	Lipoma (right)	Roentgen ray, thoracoscopy and operation	Local pain
Peery and Smith (1939)	M 14	Rhabdomyosarcoma (right)	Autopsy (roentgen ray showing hazy and irregular diaphragm)	Pain and swelling of right lower chest, cough and weight loss
Gale and Edwards (1939)	M 54	Malignant tumor (right)	Roentgen ray	Pain in right shoulder, radiating to arm and fingers
Butler (1939)	F 34	Cyst (left)	Roentgen ray	No symptom
Kinsella (1939)	F 62	Fibromyoma (right)	Operation	Mass in right lower chest
Ballon and Spector (1939)	F 45	Lipoma (left)	Autopsy	No symptoms. Mass hidden by heart and not revealed by roentgen ray

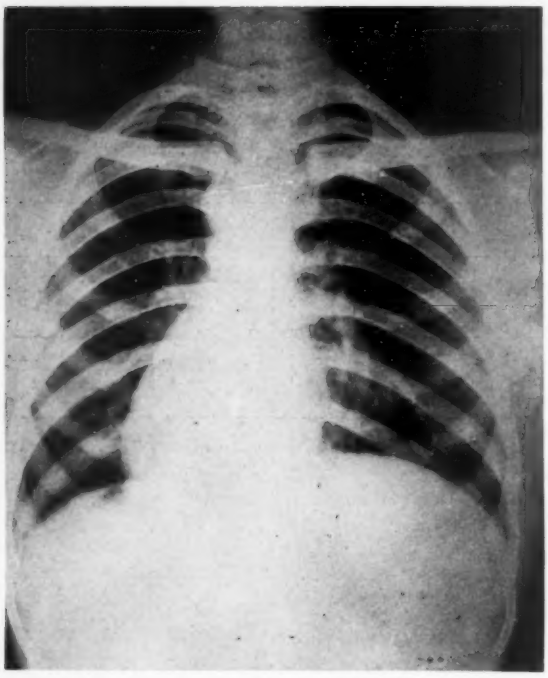

FIG. 1. Roentgenogram of chest made two years before onset of present illness.

The possibility of (1) benign tumor, (2) echinococcus cyst or (3) localized abscess was then considered. The mass was thought to be either below or in the diaphragm.

The patient was admitted to the hospital for further investigation. The general physical examination and routine laboratory studies of blood, urine and stool all showed normal findings. Repeated search for the tubercle bacillus in the sputum failed to give positive result. Intradermal test for hydatid infection was negative. Roentgen examination of the gastrointestinal tract revealed no intrinsic lesion. The nature of the diaphragmatic mass, therefore, still remained obscure.

Follow-up roentgenological examination of the chest on January 4, 1941, showed the following findings:

"The left lung is clear as before. In the right lung the pleural adhesions in the costophrenic region and the mass of the diaphragm remain unchanged since the previous examination. A definite, round, dense shadow is present in the hilus with some hazy markings in the parenchyma below it. It was present in the previous examination of December 4, 1940, although less distinct than now. It is likely that this mass represents an enlarged lymph node of the hilus."

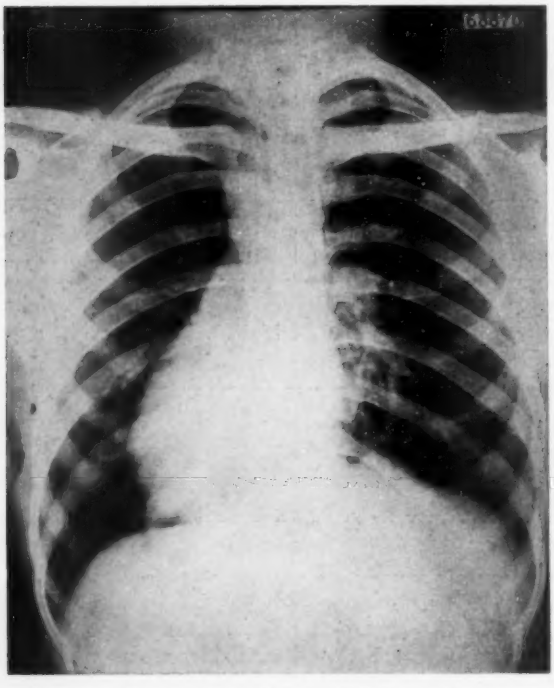

FIG. 2. Appearance of the diaphragmatic mass when first discovered.

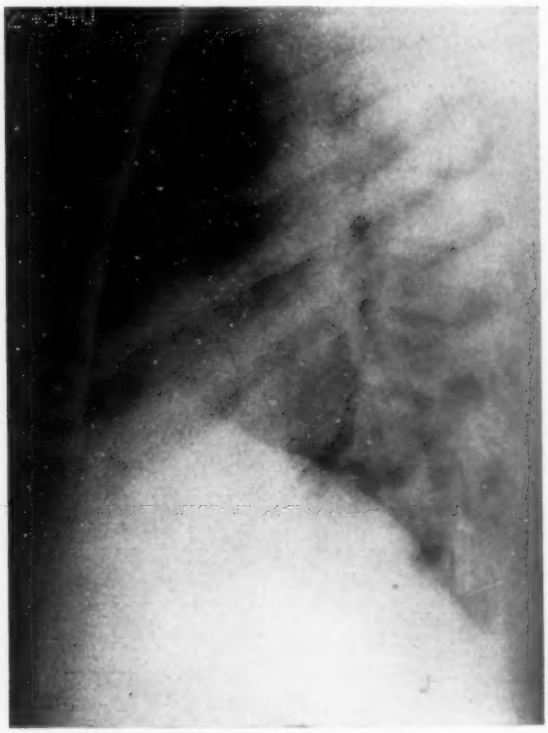

FIG. 3. Same as Figure 2, lateral view.

In view of the prominent hilar change and stationary appearance of the mass, localized tuberculous lesion of the diaphragm was considered as a strong possibility in addition to those enumerated before.

In the hope of gaining a better knowledge of its exact nature, further diagnostic procedures were carried out. Artificial pneumothorax was first tried, but failed, on account of the presence of pleural adhesions. Then artificial pneumoperitoneum was carried out on January 28, 1941, and a roentgenological examination afterwards revealed the following findings (Fig. 5 and 6):

"The lungs are as seen before. The pleural lesion of the right lower chest appears to be less marked. A moderate amount of air is present in the peritoneal cavity below the diaphragm and the air is only visualized in the upright position. The bulging in the right hemidiaphragm, as seen previously, is outlined by air as an oval mass measuring 4.7 by 3.2 cm. It is apparently attached to the right hemidiaphragm and extends both above and below the diaphragm at equal distances. The portion of the mass above the diaphragm slopes anteriorly downward from the dome. The portion below causes an indentation on the surface of the liver. The whole mass moves well with the diaphragm during respiration. It is very sharply outlined and there is no evidence of invasion into the adjacent structures. The rest of the diaphragm appears normal."

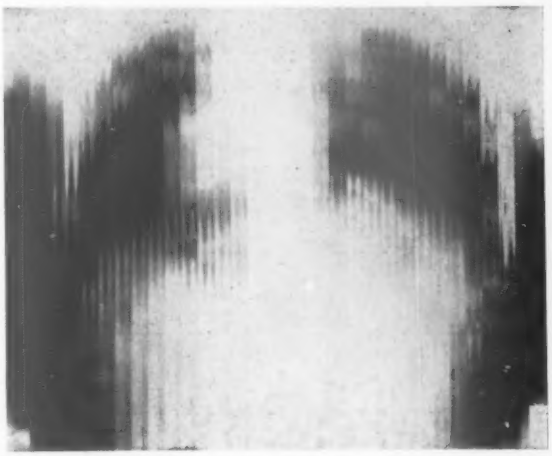

Fig. 4. Kymogram showing decreased movement of the diaphragm in the region of the mass.

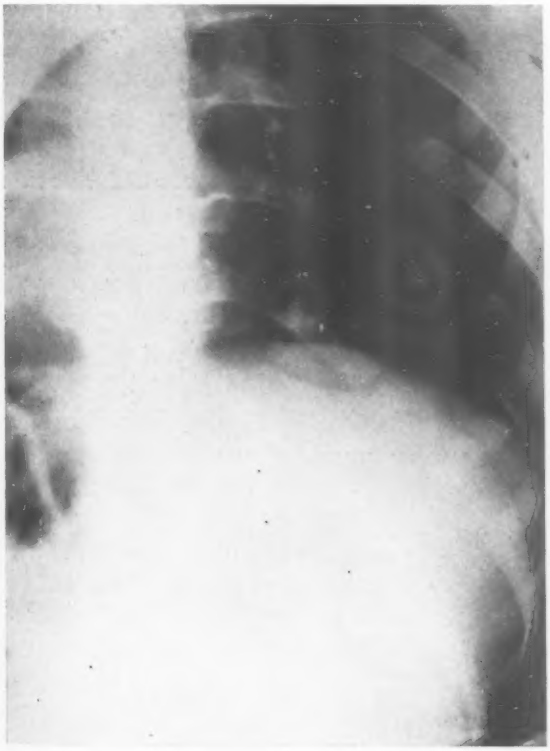

Fig. 5. Contour of the mass outlined by artificial pneumoperitoneum.

Fig. 6. Same as Figure 5, lateral view.

From the above findings, there was hardly any doubt that the mass arose from the diaphragm. On the other hand, its true nature was still unknown. The presence of obliterative pleuritis and enlarged hilar nodes presented strong evidence that the mass was inflammatory in nature. The possibility of neoplasm, however, was never ruled out preoperatively.

Operation was carried out through the thoracic route on February 15, 1941. A sharply outlined mass, measuring 4.5 cm. in diameter attached to the diaphragm was excised. The

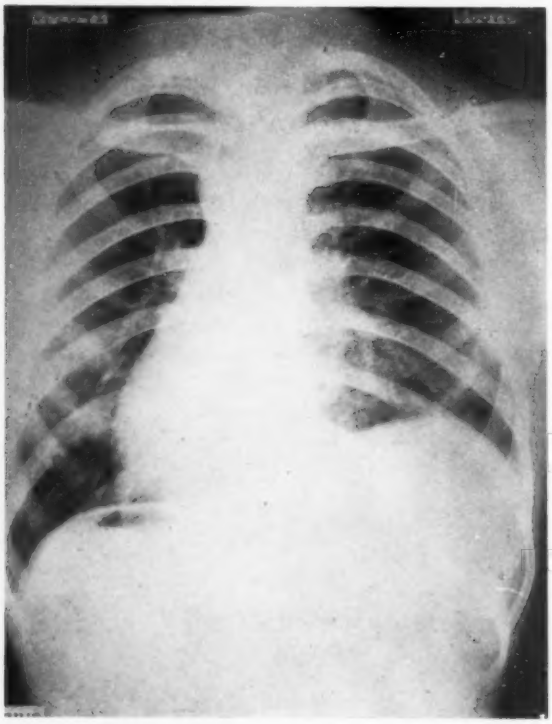

FIG. 7. Follow-up examination of the chest five months later.

postoperative course was uneventful except for accumulation of some fluid in the pleural cavity shortly after the operation. This pleural complication gradually subsided. The last follow-up roentgenological examination five months later, revealed nothing remarkable except for residual, pleural changes (Fig. 7).

On pathological examination, grossly, the mass was found to be a fluctuating, cystic tumor containing clear fluid (Fig. 8). The wall of the cyst consisted of three layers. The inner lining looked like bladder mucosa and next to it was a layer of smooth muscle. The outer layer was a fibrous serosa. Microscopically, the whole mass was tuberculous in nature.

COMMENT

A decisive, etiological diagnosis was not possible in this case in spite of the extensive study made on the patient. This was due to the rarity of such a lesion, the absence of distinctive symptoms or signs of the disease and the non-existence of associated lesions of a similar nature elsewhere in the body. The changes in the right hilar region gave some hint as to the possibility of an inflammatory lesion but the diagnosis of tuberculosis could not be made in spite of the fact that in China tuberculosis is the

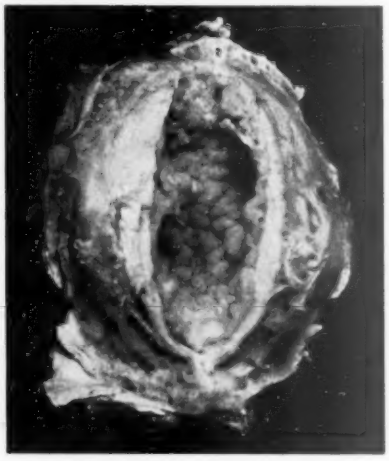

FIG. 8. Gross appearance of the specimen of the mass.

most common disease encountered in the chest. The anatomical diagnosis, in which roentgen examination played the predominating role, lay between three possibilities; namely, the growth originated from the tissues above the diaphragm, in the diaphragm or below the diaphragm. The decision was reached only with the help of diagnostic pneumoperitoneum, which clearly delineated the mass to be imbedded in the diaphragm. This conclusion proved to be correct by operation and it more than justified the effort made in the various procedures.

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REFERENCES

1. Ballon, H. C., and Spector, L. Lipoma of diaphragm. *Canad. M.A. J.*, 1939, *41*, 487–489.
2. Burvill-Holmes, E., and Brody, W. Primary angiofibroma of diaphragm. *Am. J. M. Sc.*, 1932, *183*, 679–680.
3. Gale, J. W., and Edwards, S. R. Malignant tumors of diaphragm. *J. Thoracic Surg.*, 1939, *9*, 185–193.
4. Kirshbaum, J. D. Myosarcoma of diaphragm. *Am. J. Cancer*, 1935, *25*, 730–737.
5. Peery, T. M., and Smith, W. A. Rhabdomyosarcoma of diaphragm. *Am. J. Cancer*, 1939, *35*, 416–421.
6. Söderlund, G. Beitrag zur Klinik der primären Zwerchfelltumoren besonders zur Diagnostik. *Acta radiol.*, 1937, *18*, 388–398.

THE ROENTGENOLOGICAL AND CLINICAL CORRELATION OF ACUTE ABDOMINAL DISEASE

ANALYSIS OF ONE HUNDRED CASES*

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ILEUS comes from the Greek word "ileos" meaning to twist. Dorland defines ileus as severe colic due to intestinal obstruction. It is subdivided into two types: (*a*) mechanical ileus, which is produced by mechanical obstruction, and (*b*) paralytic ileus, which is due to paralysis of the muscular coats of the intestines.

An accurate history and physical examination is essential to both the clinician and roentgenologist in making a diagnosis of ileus, and in differentiating between the two types. History and symptomatology often give more information than physical signs. The early symptoms of acute abdominal disease are intermittent crampy, colicky pain with nausea and possibly vomiting, but usually unattended by physical signs.[8] At some time during the course of an acute abdominal disease the following symptoms and signs are present: pain, nausea, vomiting, distention, rigidity, obstipation, borborygmi, absence of peristaltic sounds and collapse.

The roentgenological manifestations of acute abdominal disease include (*a*) presence of air within the intestines, (*b*) distribution of the air, (*c*) presence of fluid levels within the bowel, (*d*) presence of free air in the peritoneal cavity and beneath diaphragm, (*e*) presence of free fluid within peritoneal cavity, and (*f*) presence of abdominal distention. These manifestations must be considered as general rules only. Frequently one is able to make a diagnosis of either type of ileus from these signs. On the other hand, the signs of the two types of ileus may overlap, thereby precluding a diagnosis without the aid of the clinical findings. In a smaller percentage of cases, a definite diagnosis cannot be made even with the aid of the clinical findings. A more accurate diagnosis can always be given with a combination of clinical history, physical findings, and roentgenological manifestations.

At Cleveland City Hospital three views are routinely taken in cases of acute abdominal diseases; (1) an upright posteroanterior view of the chest to show the presence of free air beneath the diaphragm, and simultaneously any pathological process in the chest in the event subsequent surgery is done, (2) an anteroposterior view of the abdomen in a recumbent posture to show the presence and distribution of gas in the intestines, (3) a lateral supine view of the abdomen to show the presence of fluid levels and abdominal distention. These views may be made with a minimum of discomfort to the patient, and give a maximum of information.

Mechanical ileus may be acute or chronic, complete or incomplete, and located anywhere in the gastrointestinal tract. The earliest roentgenological sign of mechanical ileus is the presence of abnormal amounts of gas in the bowel. Normally a person above three years of age has little, if any, gas in the small intestine. Thus, when gas is noted, it must be assumed to be abnormal. However, a small amount of gas is normally seen in the large intestine.

The earliest sign of mechanical ileus of the small intestine is an acute "kinking" of gas filled loops of small intestine above the site of obstruction. This accumulation of gas may occur within two to four hours after onset of symptoms. Solis-Cohen and Levine[6] called this acute kinking "the hairpin turn." They believe this is the fore-

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runner of the "step-ladder" appearance of late mechanical ileus of the small intestine.

The "hair-pin turn" is succeeded by the further dilatation of segmental loops of small intestine until it becomes arranged in a step-ladder or herring-bone pattern. In this instance the long axis of the gas dilated small intestine is usually transversely situated in the abdomen, the walls separating the loops of intestine are thin, and the plicae circulares or Kerkring folds are seen transversely around the small intestine. A late sign of mechanical ileus of the small intestine is the presence of a varying number of fluid levels in the gas dilated intestine.

It is difficult to locate further the point of obstruction within the small intestine. If the dilated loops of intestine are located centrally in the lower abdomen, it can generally be assumed to be ileum, and if located in the upper abdomen, to be jejunum. The jejunum may show more clearly the plicae circulares as compared to the smoother contour of the ileum. Occasionally, this is of value in locating the site of ileus.

Incomplete mechanical ileus of the small intestine does not show gas dilated loops of intestine or fluid levels unless there has been intermittent complete obstruction.

In mechanical ileus of the large intestine, the gas is first formed in the cecum, and proceeds in an orderly fashion toward the rectum, regardless of the site of obstruction. Thus, in an early case of mechanical ileus of the sigmoid, gas may be seen along the lateral borders of the abdomen, with its long axis placed vertically in contradistinction to that of the small intestine. The intestinal walls are thick, and the haustral markings are seen transversely around the intestine, usually spaced farther apart than the plicae circulares of the small intestine. Here again the presence of fluid levels is a late sign of mechanical ileus.

The roentgenological manifestations of paralytic ileus are the presence of gas in both the small and large intestines, with their usual characteristic distribution. As a late sign, fluid levels may be present in either or both parts of the intestine. Free fluid levels may be noted in the peritoneal cavity, indicative of peritonitis. When the paralytic ileus is due to a ruptured viscus, free air may be seen beneath the diaphragm.

A roentgenological diagnosis of paralytic ileus due to mesenteric thrombosis is justified when there is continuous dilatation of the ascending and transverse colon with or without the added proof of patency of the colon by barium enema.[4]

The normal functions of peristalsis, secretion, and absorption are altered in either type of ileus.[3] Mechanical ileus causes increased peristalsis, which clinically manifests itself by colicky cramp-like pain, and increased peristaltic sounds, meteorism, or borborygmi.

Paralytic ileus is the result of splanchnic nerve irritation or paralysis, or peritoneal irritation, which may be from any cause, and is clinically expressed by absence of peristaltic sounds or the "silent belly."

In both types of ileus there occur increased secretion, decreased absorption, and failure of transportation of secretions, either because of mechanical blocking or absence of peristaltic movements.

Concomitant with and dependent upon the amount of increased secretion there is decreased absorption, and retention with stasis of the intestinal contents, and dilatation of upper small intestine and stomach. If this dilatation is not relieved, nausea and vomiting ensue.

The preceding clinical signs and symptoms, and roentgenological manifestations were utilized to attempt a clinical and roentgenological correlation of acute abdominal disease. It was also desired to demonstrate that objective interpretation of the roentgenogram was a reliable method of diagnosis and not just a "guess" or a diagnosis subconsciously influenced by the history and physical findings.

A comparison and correlation of the objective and final roentgenological interpretation, the admission and final clinical di-

agnosis, and the physical signs and symptoms were made on 100 consecutive cases of acute abdominal disease. The only criterion necessary to be included in the series was that the "three routine films" were made on the acute abdominal disease cases. The period covered was from January, 1945 through July, 1947.

TABLE I

ETIOLOGICAL CLASSIFICATION OF ILEUS

(From Eliason and Johnson[2])

I. MECHANICAL ILEUS
- A. External
  - 1. Hernias
    - a. Incarcerated
    - b. Strangulated
- B. Internal
  - 1. Hernias
    - a. Incarcerated
    - b. Strangulated
  - 2. Adhesions
  - 3. Volvulus
  - 4. Intussusception
  - 5. Neoplasm
  - 6. Strictures
  - 7. Stenosis
  - 8. Fecal impactions
  - 9. Retroverted gravid uterus

II. PARALYTIC ILEUS
- A. Reflex
  - 1. Biliary colic
  - 2. Renal colic
  - 3. Torsion, ovarian tumors
  - 4. Trauma
  - 5. Pleurisy
- B. Nerve Injury or Disease
  - 1. Spinal cord injury
  - 2. Cord tumors
  - 3. Anterior poliomyelitis
  - 4. Multiple sclerosis
  - 5. Tabetic crises
- C. Toxic
  - 1. Pneumonia
  - 2. Uremia
  - 3. Typhoid
  - 4. Systemic infections
- D. Vascular
  - 1. Mesenteric thrombosis
  - 2. Strangulation, non-intestinal
- E. Peritoneal Irritation
  - 1. Trauma at operation
  - 2. Bacterial peritonitis
  - 3. Bile peritonitis
  - 4. Acute pancreatitis
  - 5. Perforated peptic ulcer
  - 6. Hemorrhage

The objective roentgen diagnosis was one which the participating roentgenologists made with no previous knowledge of the case. The final roentgenological interpretation was one made with the aid of the admission history and physical findings as is customary at this hospital. The admission diagnosis was that of the senior house of-

TABLE II

TYPES OF DIAGNOSES

PARALYTIC ILEUS	
Appendiceal abscess	8
Viscus perforated, other than ulcer	8
Pelvic inflammatory disease	8
Peptic ulcer, perforated	7
Peritonitis	7
Mesenteric thrombosis	3
Bronchopneumonia	2
Cholecystitis and lithiasis	2
Abdominal wounds, penetrating	2
Hernia, reducible	2
Renal calculus	2
Unknown cause	2
Carcinoma, prostate	1
Encephalitis	1
Gastritis, acute	1
Menopausal syndrome	1
Psychoneurosis	1
Pancreatitis, acute	1
Carcinoma, sigmoid	1
Chest wound, penetrating	1
Postoperative	1
Diverticulitis, colon	1
Total	63
MECHANICAL ILEUS	
Adhesions, small intestine	15
Carcinoma, colon	8
Volvulus	3
Hernia, strangulated	2
Fecal impaction	1
Gallstone in ileum	1
Total	30
MISCELLANEOUS (Negative)	
Abdomen, stab wound	1
Lumbosacral strain	1
Benign hypertrophy prostate	1
Gastritis, acute	1
Cholecystitis, acute	1
Hernia, incisional	1
Disease undiagnosed	1
Total	7

ficer. The final diagnosis was the one under which the patient was discharged.

For the purpose of comparison, the final diagnosis was classified as mechanical ileus, paralytic ileus, or miscellaneous (negative for ileus) according to the etiological classification of ileus by Eliason and Johnson[2] (see Table I). The 100 cases were classified as follows: paralytic ileus, 63 cases; mechanical ileus, 30 cases; and miscellaneous, 7 cases.

Table II shows the etiological factors and the number of cases of each as listed in the above classification. The most frequent causes of paralytic ileus were appendiceal abscess, perforated viscus other than peptic ulcer, pelvic inflammatory disease, perforated peptic ulcer, and peritonitis. The most frequent causes of mechanical ileus were adhesions of small intestine and carcinoma of the colon.

For comparing the final and objective diagnoses, six members of the house staff were chosen to interpret the films objectively. Three senior house officers were chosen from the surgical and radiological departments respectively. Table III shows the correct and incorrect percentages of diagnosis for the three major classifications. The correct diagnosis for mechanical ileus was 67 per cent, for paralytic ileus 80 per cent, for miscellaneous 65 per cent, and the grand total average for all three classifications was 76 per cent. The grand total departmental average was surgery 78 per cent and radiology 75 per cent.

Table IV shows that 37 per cent of the total cases were proved as clinical diagnoses only, 58 per cent were proved by surgery, and 5 per cent were proved by autopsy. This table (IV) also shows that the final roentgenological diagnosis was correct in 90 per cent of cases of mechanical ileus, 74 per cent of cases of paralytic ileus, 30 per cent of miscellaneous cases, and 76 per cent of the total cases.

The comparison of the signs and symptoms with the final diagnosis is shown in Table V. The symptoms of nausea, vomiting and pain were common to all three classifications. The signs of tenderness, rigidity, and distention were common also. The character of the peristalsis was mentioned in only 55 per cent of the cases of

TABLE III

FINAL VS. OBJECTIVE DIAGNOSIS

Final Diagnosis	Objective Diagnosis													
	Department of Radiology						Department of Surgery						Average	
	Dr. A		Dr. B.		Dr. C.		Dr. D.		Dr. E.		Dr. F.			
	Right	Wrong	Right	Wrong	Right	Wrong	Right	Wrong	Right	Wrong	Right	Wrong	Right	Wrong
Ileus, mechanical Total—30														
No.	19	11	17	13	20	10	23	7	23	7	20	10	20	10
Per cent	63	37	60	40	67	33	76	24	76	24	67	33	67	33
Ileus, paralytic Total—63														
No.	54	9	55	8	46	17	55	8	53	10	47	16	50	13
Per cent	85	15	87	13	73	27	87	13	84	16	74	26	80	20
Miscellaneous (neg.) Total—7														
No.	3	4	5	2	7	0	3	4	6	1	4	3	4.7	2.6
Per cent	43	57	70	30	100	—	43	57	85	15	57	43	65	35
Grand Total 100 cases														
No. and per cent	76	24	77	23	73	27	81	19	82	18	71	29	76	24
Department Average			75%	25%					78%	22%				

TABLE IV

COMPARISON OF FINAL DIAGNOSIS, PROOF, OBJECTIVE READING, ROENTGENOLOGICAL INTERPRETATION, AND ADMISSION DIAGNOSIS

Final Diagnosis	Proof			Average Objective Reading		Roentgenological Interpretation		Admission Diagnosis	
	Clinical Dx	Surgery	Autopsy	Right	Wrong	Right	Wrong	Right	Wrong
Ileus, mechanical Total—30									
No.	2	25	3	20	10	27	3	27	3
Per cent	7	83	10	67	33	90	10	90	10
Ileus, paralytic Total—63									
No.	30	31	2	50	13	45	18	47	16
Per cent	46	50	4	80	20	70	30	74	26
Miscellaneous (neg.) Total—7									
No.	5	2	0	4.7	2.6	5	2	2	5
Per cent	70	30	0	65	35	70	30	30	70
Grand Total 100 cases									
No. and per cent	37	58	5	76	24	77	23	76	24

TABLE V

COMPARISON OF FINAL DIAGNOSIS, AND CLINICAL SIGNS AND SYMPTOMS

Final Diagnosis	Presence of									
	Nausea	Vomiting	Pain	Bowel Movement	Previous Operations	Rebound Tenderness	Rigidity	Distention	Peristalsis	
									Increased	Decreased
Ileus, mechanical Total—30										
No.	27	25	24	12	15	14	11	23	8	10
Per cent	90	83	80	40	50	46	36	76	22	33
Ileus, paralytic Total—63										
No.	48	36	58	49	14	28	22	33	4	12
Per cent	76	57	92	76	22	44	35	52	6	20
Miscellaneous (neg.) Total—7										
No.	3	3	6	4	2	2	3	2	1	0
Per cent	43	43	86	57	29	29	43	29	14	0
Grand Total 100 cases										
No. and per cent	78	64	88	65	31	44	36	58	13	22

TABLE VI

COMPARISON OF FINAL DIAGNOSIS AND ROENTGENOLOGICAL FINDINGS

Final Diagnosis	Roentgenological Findings				
	Gas in Intestine		Fluid Levels	Free Air	Abdominal Distention
	Small	Large			
Ileus, mechanical Total—30					
Small intestine					
No.	18	7			
Per cent	60	23			
Large intestine					
No.	9	7			
Per cent	30	23			
Total No.			22	—	16
Per cent			73	0	53
Ileus, paralytic Total—63					
No.	52	51	22	11	20
Per cent	82	80	35	17	31
Miscellaneous (neg.) Total—7					
No.	1	5	0	0	0
Per cent	14	70	0	0	0
Grand Total 100 cases					
No. and per cent	79	65	44	11	36

TABLE VII

COMPARISON OF FINAL DIAGNOSIS AND DURATION OF SYMPTOMS

Final Diagnosis	Duration Symptoms Prior to Admission								
	Hours 6 or Less	12	24	48	72	96	120	148	172 or More
	Days		(1)	(2)	(3)	(4)	(5)	(6)	(7)
Ileus, mechanical Total—30		3	2	3	6	1	2	3	10
Ileus, paralytic Total—63	11	4	7	6	9	7	4	1	15
Miscellaneous (neg.) Total—7	2	1	2	2					

mechanical ileus, but it was of interest to note that the peristalsis was decreased in 33 per cent of the cases of mechanical ileus.

The number of patients who had previous operations was divided as follows: mechanical ileus, 50 per cent; paralytic ileus, 22 per cent; miscellaneous, 29 per cent; and total cases 31 per cent.

Table VI shows the distribution of the roentgenological findings in the three classifications. An unusual feature here was that 23 per cent of the cases of mechanical ileus of the small intestine showed gas in the large as well as small intestine. Fluid levels were present much more commonly in mechanical than paralytic ileus.

Table VIII shows that the total cases were about equally divided between the male and female sex. Mechanical ileus was more prevalent between fifty and sixty-five years of age. Paralytic ileus showed no special age distribution.

TABLE VIII

COMPARISON OF FINAL DIAGNOSIS, AND SEX, AND AGE INCIDENCE

Final Diagnosis	Sex		Age—Figured to Closest 5 Year Level															
	M	F	5	10	15	20	25	30	35	40	45	50	55	60	65	70	75	80
Ileus, mechanical Total—30	16	14	—	—	—	1	3	1	2	—	—	5	2	5	5	2	2	2
Oleus, paralytic Total—63	35	28	1	—	2	5	2	8	2	3	6	7	5	7	4	5	4	2
Miscellaneous (neg.) Total—7	4	3	—	—	1	1	—	1	1	—	—	1	—	1	1	—	—	—
Grand Total 100 cases	55	45	1	—	3	7	5	10	5	3	6	13	7	13	10	7	6	4

The duration of symptoms is shown in Table VII. The cases of mechanical ileus had a duration of from twelve hours to seven days or more, with the latter group having the greatest number of cases. Cases of paralytic ileus showed an even distribution of the duration of symptoms ranging from six hours to seven days or more.

FIG. 1. Case 1. Early mechanical ileus of small intestine. Note "hair-pin" loop of gas distended small intestine located in the epigastrium.

CASE REPORTS

CASE I. C. W., a twenty-four year old colored male, was admitted with a chief complaint of abdominal pain. Forty-eight hours prior to admission, he began having sudden, crampy, generalized abdominal pain with some associated nausea and vomiting. The bowel movements were normal. The patient had a ruptured appendix drained four years previously. Slight tenderness was present in the right lower quadrant of the abdomen. There was no abdominal distention or rigidity and no borborygmi were heard.

The roentgenograms showed a "hair-pin loop" of small intestine located in the epigastrium, some gas in the ascending colon and occasional fluid levels on the lateral view (Fig. 1). The lateral view was omitted because of inability to reproduce it satisfactorily. The clinical and roentgenological diagnosis was mechanical ileus of the small intestine. Exploratory laparotomy confirmed this diagnosis as several ahesion bands were found in the ileum.

CASE II. I. W., a sixty-three year old colored

female, was admitted with a chief complaint of persistent vomiting of three days' duration. The vomitus was not of fecal character, but was associated with crampy abdominal pain. The patient had a caesarean section many years ago. The abdomen was moderately distended, rigid and diffuse abdominal tenderness with some rebound tenderness was noted. No visible peristalsis or borborygmi were present.

The roentgenograms revealed distention of the small intestine with gas, and a "stepladder pattern" was seen (Fig. 2). No gas was noted in the colon. The lateral view showed only a few fluid levels within the small intestine, but no abdominal distention.

The clinical and roentgenological diagnosis was mechanical ileus of the small intestine. Exploratory laparotomy revealed adhesion bands in the mid ileum.

Fig. 2. Case II. Later stage of mechanical ileus of small intestine. Note "stepladder" pattern, and transverse arrangement of small intestine.

Case III. C. H., a fifty-four year old colored male, began having cramps in the epigastrium seven days prior to admission; these became progressively worse and for the past five days had been projectile in nature. There were three small bowel movements in the past week. The patient had a gallbladder operation thirty years ago. The abdomen was moderately distended, rigid, showed marked tenderness and borborygmi were present.

The roentgenograms showed distention of the small intestine with gas. Abdominal distention and many fluid levels were noted on the lateral view (Fig. 3).

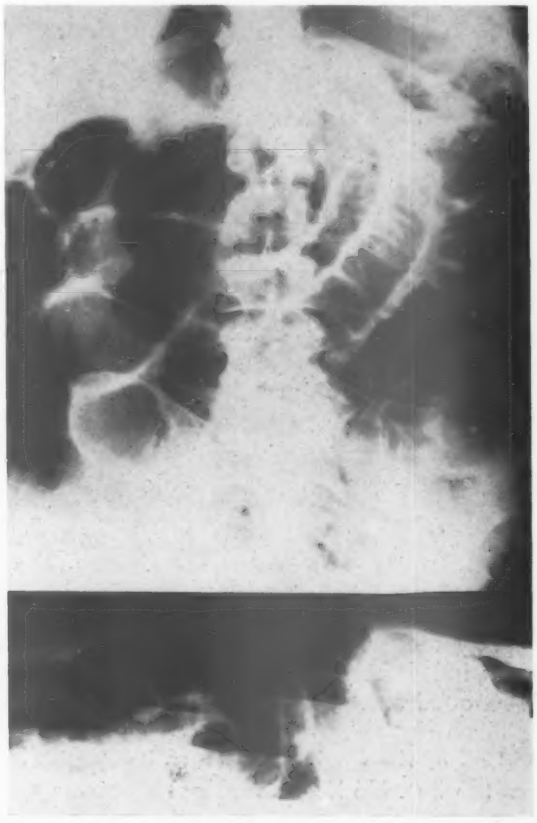

Fig. 3. Case III. Late stage of mechanical ileus of small intestine. Note the "stepladder" pattern, and plicae circulares of the small intestine. Many fluid levels can be seen on the lateral view.

The clinical and roentgenological diagnosis was mechanical ileus of the small intestine. Exploratory laparotomy revealed adhesion bands around the terminal ileum and attached to the anterior abdominal wall.

Case IV. T. W., a four month old white male, was in good helath until twenty-four hours prior to admission. Then he became listless and fretful. There were abdominal cramps. The stools were brown, liquid and contained flecks of bright red blood. The abdomen was distended,

FIG. 4. Case IV. Mechanical ileus due to intussusception. There is gas in stomach and dilatation of all of small intestine. No gas is noted in colon.

slightly tender and peristalsis was normal. A mass, indefinitely outlined, was felt in the right lower quadrant.

The roentgenograms revealed the stomach and all of the small intestine to be dilated by gas (Fig. 4). No large intestinal dilatation was noted. A barium enema showed good filling of the colon to the hepatic flexure. Then multiple "ring filling defects" were seen in the ascending colon (Fig. 5).

The clinical and roentgenological diagnosis was mechanical ileus due to intussusception. Exploratory laparotomy showed the terminal ileum to be intussuscepted into the ascending colon for a distance of about 4 inches.

CASE V. M. J., a sixty-six year old white female, was admitted with a chief complaint of pain in the stomach and weight loss. Vague abdominal pain and weight loss began a few months prior to admission. There were several episodes of diarrhea alternating with constipation, but no bloody or tarry stools were seen. Two weeks prior, nausea, vomiting and crampy abdominal pain started. There was abdominal distention, which was more pronounced on the right side. Moderate tenderness was present in the right lower quadrant. There was no rigidity of abdomen or hyperactive peristalsis.

The roentgenograms revealed a marked distention of cecum and ascending colon (Fig. 6). Numerous dilated loops of small intestine were present, but no fluid levels were seen.

The clinical and roentgenological diagnosis was mechanical ileus of the large intestine. A cecostomy was performed. At this time a hard, nodular mass was palpated in the hepatic flexure of the colon. Biopsy was not obtained. The patient died and autopsy was not done.

CASE VI. E. T., a sixty-three year old white female, was transferred from the psychiatric division with a chief complaint of abdominal pain. No other history could be obtained. The abdomen was markedly distended and bulging in the flanks. Occasional peristaltic waves were seen, the abdomen was tympanitic, but no bor-

FIG. 5. Case IV. Mechanical ileus due to intussusception. Barium enema shows multiple "ring filling defects" of ascending colon.

borygmi were heard. No masses or tenderness was noted.

Roentgenograms revealed marked distention of the entire colon located obliquely in the abdomen. Subsequent barium enema showed the same dilatation of the colon. There was complete occlusion in the sigmoid region and no barium flowed past this point (Fig. 7). A gallstone was seen in the right upper quadrant.

The clinical and roentgenological diagnosis was mechanical ileus of the large intestine due to volvulus. A cecostomy was performed. Twelve days later an exploratory laparotomy revealed only a very redundant normal sigmoid colon. A cholecystectomy was done at this time. The final diagnosis was mechanical ileus of colon due to volvulus and cholelithiasis.

Case vii. F. S., a sixty-eight year old white male, was transferred from the psychiatric division because of marked abdominal distention. No history was available. The abdomen showed marked distention, moderate tenderness

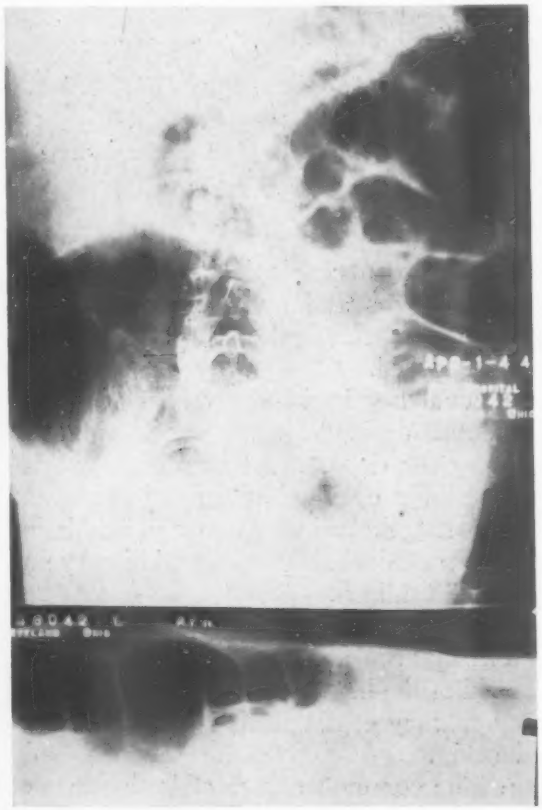

Fig. 6. Case v. Mechanical ileus of large intestine due to carcinoma of hepatic flexure. Note large dilated cecum.

Fig. 7. Case vi. Mechanical ileus of large intestine due to volvulus. Marked distention of large intestine located obliquely in abdomen. Barium enema shows complete occlusion in sigmoid colon.

and no rigidity. A few peristaltic sounds were heard.

Roentgenograms revealed marked dilatation of the ascending and transverse colon. The small intestine was dilated with gas also (Fig. 8). On the lateral view, free air was noted in the peritoneal cavity, which was also seen on the chest roentgenogram. No fluid levels were present.

The clinical and roentgenological diagnosis was mechanical ileus of the large intestine, with perforation of the cecum and subsequent paralytic ileus.

Exploratory laparotomy revealed a large amount of free air in the peritoneal cavity. An enormously dilated ascending and transverse colon was seen. A perforation 2 cm. in diameter was located in the cecum. A hard, firm, nodular, constricting mass was palpated in the sigmoid colon. A cecostomy was done. The patient died fourteen days postoperatively and no autopsy was done. The final diagnosis was mechanical ileus of the colon due to carcinoma and paralytic ileus due to perforation of the cecum.

FIG. 8 Case VII. Mechanical ileus of large intestine due to carcinoma of sigmoid colon. Note marked distention of cecum and transverse colon. Gas dilated small intestine is present also. On the lateral view free air in the peritoneal cavity can be seen outlining loops of gas dilated intestine.

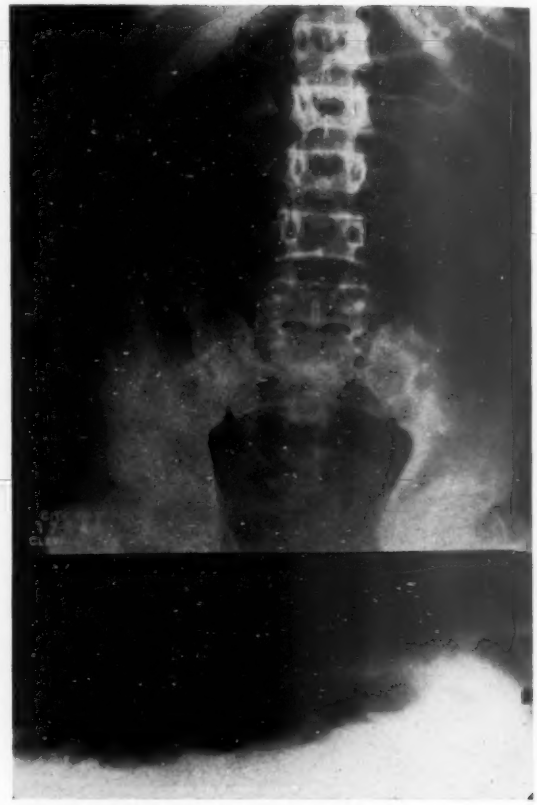

FIG. 9. Case VIII. Paralytic ileus due to trauma. Note gas dilated loops of both small and large intestine. No fluid levels are seen on lateral view.

CASE VIII. A. LeM., a sixteen year old colored male, was admitted with a gun shot wound in the right flank. Six hours prior, the patient was shot with a pistol. There was a through and through bullet wound of the right flank, with the point of entrance and exit anterior and posterior respectively. The abdomen was soft, nontender, non-rigid, not distended and no peristaltic sounds were heard.

Roentgenograms revealed moderate distention of several loops of the small intestine (Fig. 9). Gas and fecal material were noted throughout the colon. No fluid levels were seen on the lateral view.

The clinical and roentgenological diagnosis was gun shot wound of the right flank and paralytic ileus. Exploratory laparotomy revealed the tract of the wound to be superficial without extension into the peritoneal cavity. The appendix was removed. The final diagnosis was gun shot wound of the right flank and paralytic ileus due to trauma.

SUMMARY

1. The roentgenological manifestations, physical signs and symptoms, and physiology of mechanical and paralytic ileus are discussed.

2. One hundred consecutive cases of patients examined for acute abdominal disease by the department of radiology were selected for comparison of objective and final roentgenological diagnoses, admission and final clinical diagnoses, and history and physical findings.

3. Objective roentgenological diagnosis is a fairly accurate method. However, with the aid of the history and physical findings, the accuracy of diagnosis is increased considerably.

4. The common causes of both types of ileus are shown.

5. Roentgenological examination should be made on all cases of suspected acute

abdominal disease as this may aid the surgeon in making a decision to operate immediately or to follow a conservative plan of treatment.

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REFERENCES

1. Dorland, W. A. N. The American Illustrated Medical Dictionary. Seventeenth Edition. W. B. Saunders Company, Philadelphia, 1937.
2. Eliason, E. L., and Johnson, J. Diagnostic features of ileus. *Radiology*, 1936, *26*, 342–348.
3. Ochsner, A. Physiologic considerations of ileus. Am. J. Roentgenol. & Rad. Therapy, 1937, *37*, 433–445.
4. Rendich, R. A., and Harrington, L. A. Roentgenologic observation in mesenteric thrombosis. Am. J. Roentgenol. & Rad. Therapy, 1944, *52*, 317–322.
5. Sante, L. R. Intestinal obstruction. Am. J. Roentgenol. & Rad. Therapy, 1935, *34*, 744–754.
6. Solis-Cohen, L., and Levine, S. X-ray diagnosis of complete and partial acute intestinal obstruction. *Radiology*, 1938, *31*, 8–14.
7. Stecher, W. R. Roentgenologic aid in "acute abdomen," with special reference to intestinal obstruction. *Radiology*, 1936, *26*, 729–740.
8. Wangensteen, O. H. Elaboration of criteria upon which early diagnosis of acute intestinal obstruction may be made, with special consideration of value of x-ray evidence. *Radiology*, 1931, *17*, 44–62.

GAUCHER'S DISEASE IN BONE

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THE bone lesions of Gaucher's disease are due to infiltration and replacement of bony trabeculae by kerasin-bearing reticulum cells or so-called Gaucher's cells. Gaucher's disease is a rare, familial, constitutional disorder of lipoid metabolism as a result of which kerasin, a product of the incomplete breakdown of complex lipoids, is stored in the reticulum cells of the "lymphatic-hematopoietic system." Despite the widespread distribution of these vulnerable reticulum cells and histiocytes throughout the body, Gaucher cells have been found only in the spleen, liver, bone marrow and lymph nodes; not in any other organs. The clinical manifestations of Gaucher's disease include: great enlargement of the spleen, enlargement of the liver, brownish pigmentation of the exposed parts of the skin, wedge-shaped thickening of the conjunctiva near the cornea (pinguecula), marked hemorrhagic tendency, leukopenia and thrombocytopenia. The diagnosis is established by splenic or bone marrow puncture or by splenectomy. *Symptoms occur in childhood and adolescence, but because of its chronicity and slow progression, patients with Gaucher's disease may live a fairly normal life for many years.*

Although the disease was first described by Gaucher in 1882 (erroneously as an epithelioma), it was not until 1904 that Brill *et al.* noted Gaucher cells in the bone marrow in autopsy material. Microscopically these cells may appear as minimal collections, nodules, or as a diffuse infiltration in the marrow. The degree of this pathological cellular infiltration will determine the primary quality and extent of the related gross roentgenographic lesions. On the basis of these roentgenographic bone lesions and the clinical criteria mentioned above, a presumptive diagnosis of Gaucher's disease may be made.

Pick (1937), who suggested that the predisposition to gross skeletal changes may also be familial, noted (1922) such gross skeletal changes as gibbus, pathological fractures of long bones, palpable bony thickenings and deformity of the hips. Klercker (1926), in conjunction with Junghagen, made the first detailed report on the roentgenographic changes observed in a three year old female with Gaucher's disease. The thirteen figures illustrating this article showed successively a coxa valga (probably congenital and the only one of its kind in the literature with Gaucher's disease), followed by changes resembling early Perthes' disease of the femoral head, worm-eaten appearance of the femora and broadening below, atrophy and growth arrest lines of the upper tibiae and fibulae, worm-eaten appearance of one humerus, and flattening of the vertebral bodies both in the sagittal and frontal planes at the dorsolumbar levels, together with coarseness of the trabeculae and slight narrowing of the disc between the twelfth dorsal and first lumbar vertebrae. The English summary of this article stressed: (1) well marked general deficiency of the calcium contents (atrophy); (2) the coarse and porous nature of the spongious trabeculae; (3) the destruction of the spongious tissue, either in smaller well defined areas, giving to the bone a worm-eaten appearance, or in larger areas, leading to more extensive defects, and (4) the apparent immunity or lack of change in the periosteal and cartilaginous structures.

In the same year, Case 2, a female, aged thirty-four, was reported by Cushing and Stout and the article was illustrated by roentgenograms of the pelvis. In Figure 4, three years after onset of hip symptoms, the pathological changes appeared chiefly as an irregularity in the acetabulum. Figure 5 showed atrophy and decrease in the size of the affected femoral head and neck

(three months after splenectomy). In this case the femoral head and several "sequestrums" were resected. The microscopic examination of these specimens revealed the bone marrow to be packed with Gaucher cells, many of them being elongated and narrowed. Unfortunately the "sequestra" could not be clearly identified for the pathological examination. Since this is the only case on record with hip involvement in which definitive operative treatment was afforded a victim of Gaucher's disease in bone, a valuable opportunity was lost to study these necrotic fragments. Interestingly enough, the microscopic examination of the capsular structures in this case showed only thickening, thus indicating the absence of parosteal reaction or participation of the disease outside the marrow cavity. However, Potter and McRae (1933), in reporting upon a case of Gaucher's disease (Case 2) of the lower femur which was operated upon erroneously for chronic osteomyelitis, noted that there was an *edema of the periosteum* and that the marrow cavity was filled with a gelatinous, chocolate-colored fluid from which was removed a small sequestrum.

In 1929, Welt *et al.* reviewed the literature and reported 11 cases of Gaucher's disease, 6 of which showed related roentgenographic changes. The clinical symptoms in those cases with bone changes included pain, stiffness and limp. In the acute stages there was swelling, bone tenderness, occassional redness and limitation of motion; which may lead to an erroneous diagnosis of osteomyelitis. All the bones except the skull were involved in their series. There was 1 case with gibbus and 3 with pathological fractures. All of the latter healed subsequently. They confirmed Pick's observation that the disc is not involved in spinal Gaucher's disease. In this connection, it is to be remarked that Melamed and Chester (1938) found a third lumbar herniated disc at autopsy in their case. The disc in this instance was highly vascularized and the nucelus pulposus partially fibrotic. Welt *et al.* also described areas of rarefaction and condensation giving a mottled appearance to the bone; coxa vara and mushrooming of the femoral heads and fusiform expansion of the lower femora bilaterally. The latter they considered to be characteristic of the disease which results in a club-shaped widening of the lower femora, especially toward the medial condyles. They summarized the roentgenographic changes to be: mottling, at times condensation, expansion of bone, lack of demarcation between marrow and cortex and a marked thinning of cortex.

Schein and Arkin (1942) also stressed the hip changes in Gaucher's disease. They explained that under the influence of weight bearing, the primary infiltrative changes may be supplanted by secondary collapse and aseptic necrosis of the femoral head with absorption of the acetabulum. They referred to Reiss and Kato's (1932) observation that the disease may mimic chronic osteomyelitis, tuberculous coxitis and Perthes' disease in children; and they referred also to the late osteoarthritic changes which occurred in Determan's (1932) case. In their series, 8 out of 20 cases of Gaucher's disease (19 verified) manifested hip involvement. Hip involvement was second in frequency to lower femoral lesions which were found in two-thirds of the cases. They classified hip lesions as follows: (A) Hip lesions in children, in which the changes in the femoral heads usually suggested Perthes' disease or early tuberculous lesions. Secondly, changes in the femoral necks denoting simple infiltration, pathological fracture or coxa vara deformity with broadening and irregularity of the epiphyseal line, the latter suggesting epiphysiolysis which might be secondary to simple infiltrative changes or pathological fracture. (B) Hip lesions in adults accompanied by signs and symptoms of osteoarthritis; probably secondary to childhood lesions. Secondly, similar changes in young adults, but without any symptoms or signs pointing to the hip; it being presumed that such signs and symptoms would eventuate.

More recently (1948), Arkin and Schein discussed aseptic necrosis as a significant factor in Gaucher's disease of bone. They reviewed 5 cases affecting the spine, hips, lower femora, and upper tibiae, and stated that the infiltration of Gaucher's cells around the small arteries and capillaries is sufficient to produce aseptic necrosis.

CASE REPORT

Lorena S., white female, unmarried, aged twenty-seven, was referred for orthopedic examination in November, 1936, by Dr. Gregg Thompson after he had established the diagnosis of Gaucher's disease, by splenectomy* at St. Joseph's Hospital on December 18, 1934. She remained relatively well thereafter until she developed low back pain and "sciatica" on the right side two weeks before my examination. At that time the physical and roentgenographic examination (Fig. 1*A* and *B*) was essentially negative except for tenderness over the right sacroiliac joint. Her symptoms were nevertheless considered to be osteocopic in origin as a result of minimal osseous Gaucher's disease. While in the hospital she ran a *low grade fever*. Pertinent laboratory findings at that time were 234,000 platelets, a mild anemia and a moderate leukocytosis. She was relieved after three days of Russell traction, and except for two brief periods of hospitalization—on March 24, 1937, for "exophthalmic goiter" and on May 20, 1937, for "pericardial effusion"—she remained relatively well.

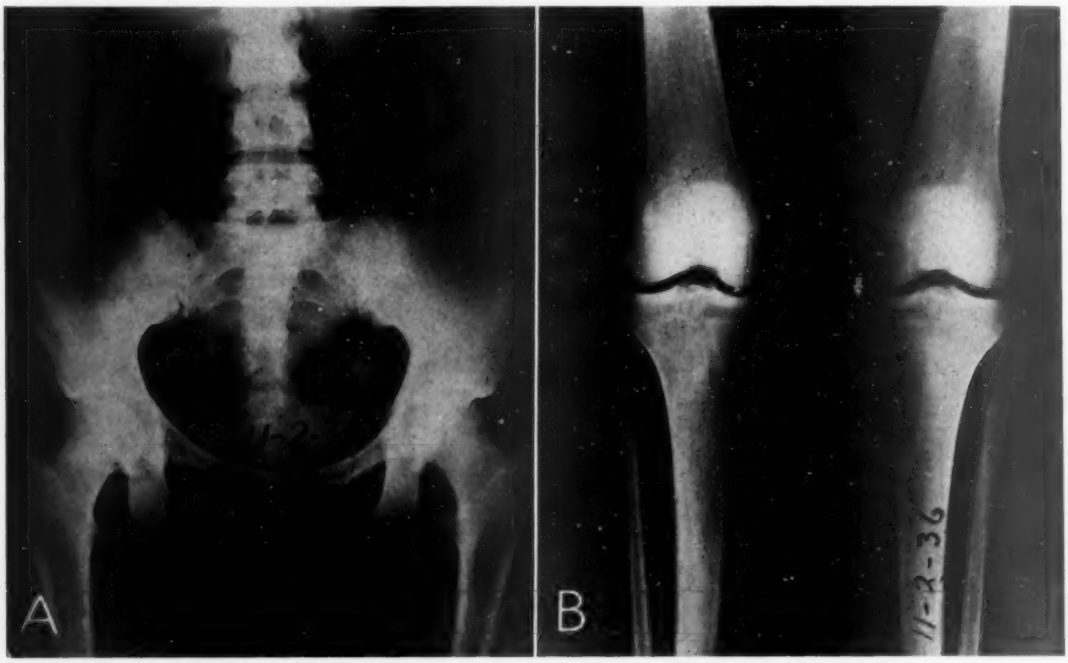

FIG. 1. (*A*) Pelvis of patient, November 2, 1936, two weeks after onset of low back pain and right sciatica and two years after splenectomy. (*B*) Knees at same time.

In October, 1937, she slipped and fell in her kitchen. An increasingly painful disability of the left hip forced her to seek orthopedic attention several days later. Roentgenographic

* Pathological Report: Dr. William J. Hunt, pathologist, St. Joseph's Hospital, November 1934. *Gross Examination:* The spleen . . . weighing 2750 grams, is pale to deep brick red color. . . . Cut section is moderately firm. . . . *Histological Examination:* . . . A large portion of the tissue consists of masses of large round, oval or polygonal cells—the so-called Gaucher cells. . . . The protoplasm of these Gaucher cells has a hyaline and finely fibrillar appearance, and takes the stain very feebly. Many cells have a vacuolated or foamy appearance. . . .

In many areas the Gaucher cells occupy the greater part of the pulp and are arranged diffusely in irregular alveoli or trabeculae. The supporting fibrous tissue matrix shows Gaucher cells singly and in small groups and columns. The blood spaces are lined by cells, many of which resemble the Gaucher cells. . . . Many of the blood sinuses are compressed by the hyperplastic cell tissues, ... The increase in the size of the spleen results from the swollen hyperplastic reticulo-endothelial cells and the dilated blood spaces, rather than the fibrosis which appears to be secondary pathological change. . . .

Pathological Diagnosis: Gaucher's splenomegaly.

examinations of the hip at that time showed a transcervical fracture with varus deformity.* This was presumed to be a pathological fracture despite the absence of other pathological findings. On this account, a conservative (Leadbetter technique) reduction and retention in a plaster spica was done under spinal anesthesia. Another roentgenographic examination two months later showed a recurrent varus position of the fragments, still without evidence of Gaucher's disease. It was felt, therefore, that open reduction and internal fixation should be attempted. As was to be expected the coagulation time was nine to ten minutes, and the bleeding time was one and one-half minutes. The platelets were 319,920, the red blood cell count 3,780,000 and the white blood cell count 18,500. She was given 500 cc. of whole blood before operation and a similar transfusion after operation. On December 16, 1947, under spinal anesthesia, the affected hip joint was exposed by Smith-Petersen's technique.

A very firm impaction of the fragments, wholly unsuspected from the appearance of

Fig. 2. Changes noted, same patient, May 26, 1938, about six months after fracture of left femoral neck.

the roentgenograms, was thereupon found. In the face of this situation it was deemed unwise to do anything else. A biopsy was taken from

* Unfortunately these original roentgenograms, as well as several rechecks taken subsequently, have been lost. Reports made then by Dr. A. B. McGlothlan, staff roentgenologist, failed to note any evidence of pathological changes to account for the patient's obvious pathological fracture.

Fig. 3. Changes noted, same patient, July 10, 1939.

the synovial and capsular tissues about the fracture site.† Closure was made without drainage and traction applied. The immediate convalescence was uneventful. She made a good clinical recovery following subsequent plaster fixation and was mobilized about six months after operation. At this time the available roentgenograms (dated May 26, 1938, Fig. 2) showed rather widespread changes; the most notable of which were: diffuse areas of decreased and increased density of the left iliac wing, "unhooking" of the right pubic bone at the symphysis, obliterative changes in the sacroiliac regions, early deformity of the left femoral head superiorly, increased density and ad-

† *Gross Examination:* (Dr. William J. Hunt). The tissue is a very soft fragment of red to white tissue 1.5 by 1 by 0.5 cm., slightly granular with elongated fibrils apparent in some portions. There is a slight smoothing of the surface tissue, white at one point.

The second tissue grossly resembles the first, consisting of white fibrotendinous or fascia-like material intermixed with redder tissue measuring 2.2 by 2 by 0.7 and 1.5 by 1 by 0.7 cm. True membrane surface is not identified in the latter tissue.

Histological Pathology: Some tissue consists of fibrocollagenous and fibroreticular tissue traversed by vessels of varying type. The smaller vessels at times are surrounded by collars of round cells including some forms which were possibly of plasma cell type. The endothelial cells lining capillaries were not quite prominent and hyperplastic. Blood pigment was freely but irregularly distributed through the tissue; occasionally the clumps of round cells became quite prominent and almost follicular in type. At one point there was an attempt at irregular layering such as may be observed in pseudosynovial or bursal-like structures. Endothelial cells were not present in any unusual numbers and did not present any indication of unusual morphological or metabolical changes. There is no definite indication of specific inflammatory reaction.

Tissue removed from the scar zone consists essentially of atrophic voluntary muscle, fatty areolar tissue and irregular paralleling deposits of dense fibrocollagenous tissue not unlike that found in fascia and fasciotendinous tissue. There is no definite indication of inflammatory reaction. *Pathological Diagnosis:* Synovitis chronic (possibly traumatic). Scar tissue.

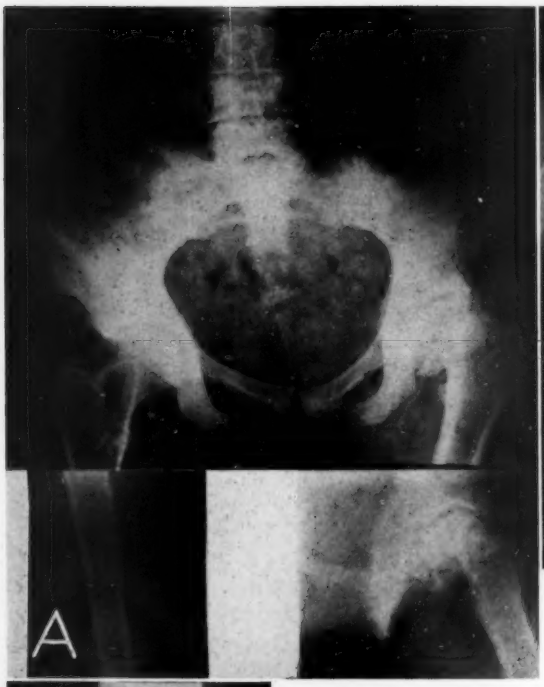

FIG. 4. (*A*), (*B*) and (*C*). Changes noted, same patient, January 22, 1948.

vanced healing of the fracture of the left femoral neck in varus and a slight flaring of the inferior lateral margins of the fourth lumbar vertebra.

In the next ten years, the patient, except for a brief period of hospitalization on March 13, 1943, for "pleurisy," and an increasing deformity of the left hip, remained relatively well and continued to work as a secretary. A routine roentgenogram taken on July 10, 1939 (Fig. 3) showed an increased lateral expansion of the lower border of the fourth lumbar vertebra. The right sacroiliac joint was practically obliterated, as was the left. The supracotyloid bone on the left was mottled, with areas of increased condensation. The left hip joint was obliterating but the acetabular margin seemed resistant to the disease process. The left femoral head had become almost entirely necrotic and was fixed to the slightly widened neck in varus. There was a fixed "unhooking" at the symphysis, and increased condensation of the medial trabecular system of the left femoral neck.

On January 22, 1948, the patient was prevailed upon to have a roentgenographic checkup although she was symptom free at that time. Roentgenograms of the right knee and leg (Fig. 4*C*) failed to show the so-called typical widening of the lower femur. The pelvis (Fig. 4*A*) showed marked osteoarthritic changes of the fourth and fifth lumbar vertebrae and diminished disc spaces. The right sacroiliac joint had become fused, the left was not. The left hip had progressed to complete disintegration of the femoral head with a loose portion inferiorly. The left acetabular margin was only

slightly deformed and the joint space was still present. The left femoral neck was broadened. The left and right supracotyloid bones were similarly and slightly mottled. The iliac wings were practically normal.

Most remarkable were the changes in the right upper femur and neck. Here there was a central oval cyst at the base of the neck surrounded by an extensive septate demineralization and mottling which involved the trochanteric and subtrochanteric areas of the femur. The cortices as compared with the left side were markedly thinned.

The patient was advised of an impending pathological fracture of the right hip.

Twenty-five days later, while at work and washing her hands, she twisted her body, heard a loud snap in the right hip, fell to a sitting position and was unable to get up due to severe pain in the right hip. On admission to the hospital (February 17, 1948), the pertinent physical findings were: long standing emaciation, systolic apical murmur, a nodule in each axilla and mild enlargement of the liver. The laboratory examinations were not especially remarkable. Roentgenographic examination showed an oblique pathological fracture at the base of the right femoral neck with slight varus deformity (Fig. 5). Due to the shortening occa-

Fig. 5. Changes noted, same patient, February 17, 1948.

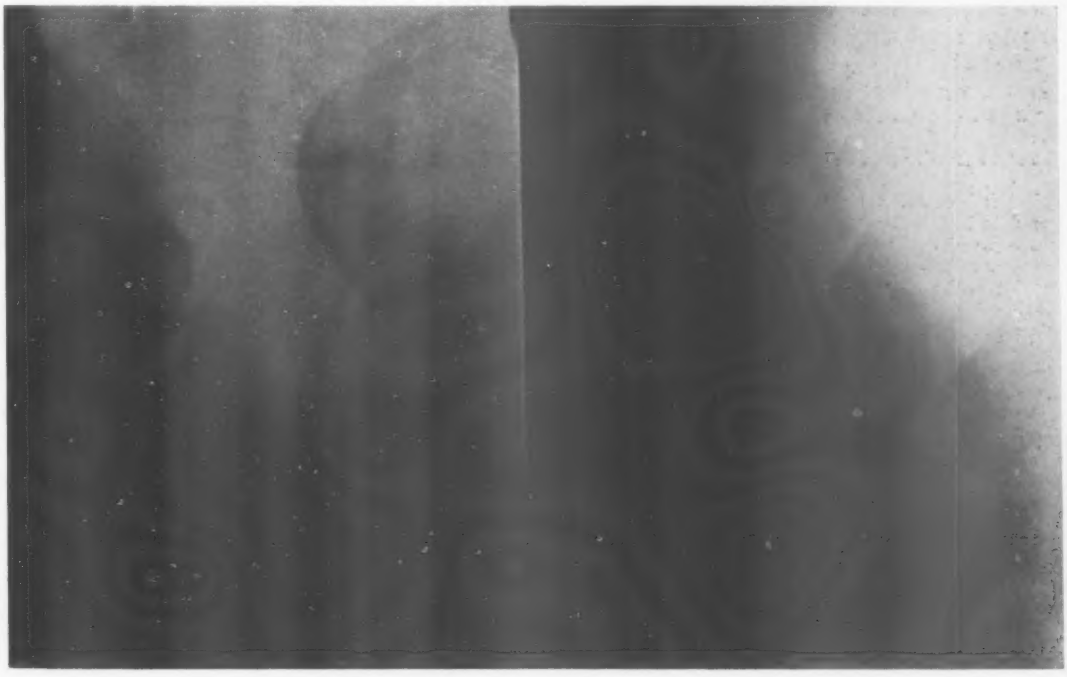

Fig. 6. Same patient, February 24, 1948, in traction.

FIG. 7. Same patient, before weight-bearing.

sioned by the old flexion adduction deformity of the left hip, a McMurray osteotomy was considered in order to help equalize the lower extremities. The patient preferred conservative treatment, which consisted of traction (February 17, 1948) and spica casts (February 28, 1948 to May 20, 1948). At her urgent request a corset was applied and crutch mobilization begun about five months after injury. She returned to work on crutches about one month later.

In Figure 6, it appears that the pathological fracture had initiated regressive changes in the pathological process. There was gradual increase in density and blurring out of the septate area of absorption. The pelvifemoral angular relationships remained mechanically sound (Fig. 7) until after she had begun guarded crutch weight-bearing following which (Fig. 8*A* and *B*) a definite increase in varus occurred.

Comment. Certain features of this case may be translated into general clinical values in regard to Gaucher's disease. In the first place, the chronicity and periodicity of the underlying pathological process is to be remarked. This was expressed in the patient's emaciation, the successively related local manifestations and varying intervals of comparative freedom from symptoms. Therein is apparent a curious paradox between central constitutional cause and centrifugal local effect. In other words, we have a situation, with the probable exception of the splenomegaly, whereby an irreversible physiopathological process may produce more or less reversible local manifestations.

Heilbron (1935) is credited by Bloem

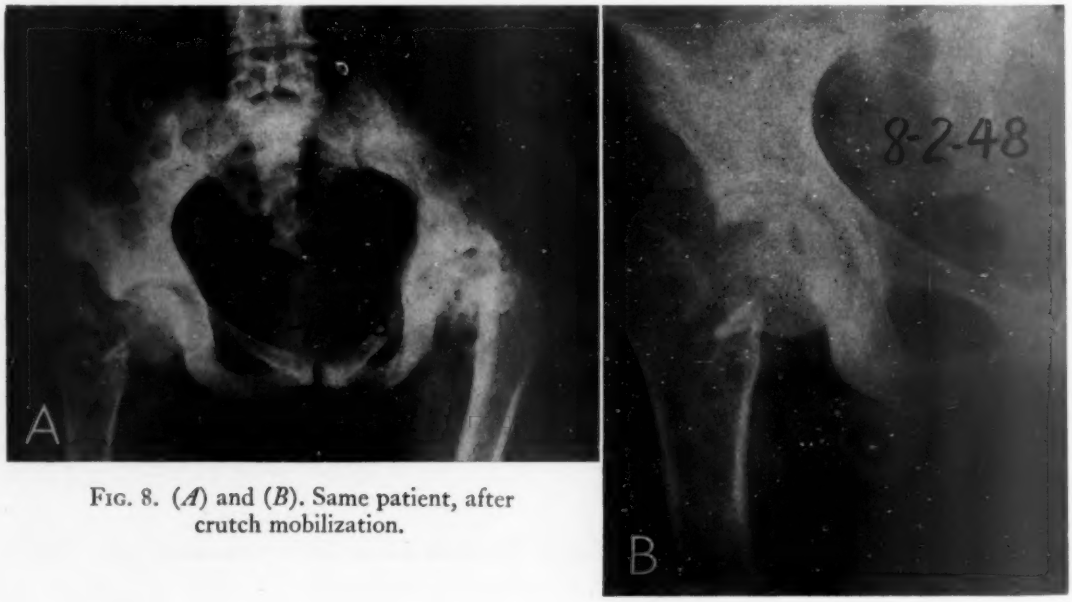

FIG. 8. (*A*) and (*B*). Same patient, after crutch mobilization.

et al. with having reported a case of Gaucher's disease in a child in whom the osseous lesions cleared up. The regressive nature of the bone lesions in the case under discussion, in those areas not subjected to severe stress (iliac wings, for instance) is to be remarked. The fact that kerasin is chemically inert helps to explain the chronicity tivity of the reticuloendothelial system its reposition is long delayed or stopped altogether. Thus this patient recovered spontaneously from "exophthalmic goiter," "cardiac effusion" and "pleurisy," and from recurrent attacks of tonsillitis, following tonsillectomy (1936). A negative therapeutic attitude is therefore not warranted;

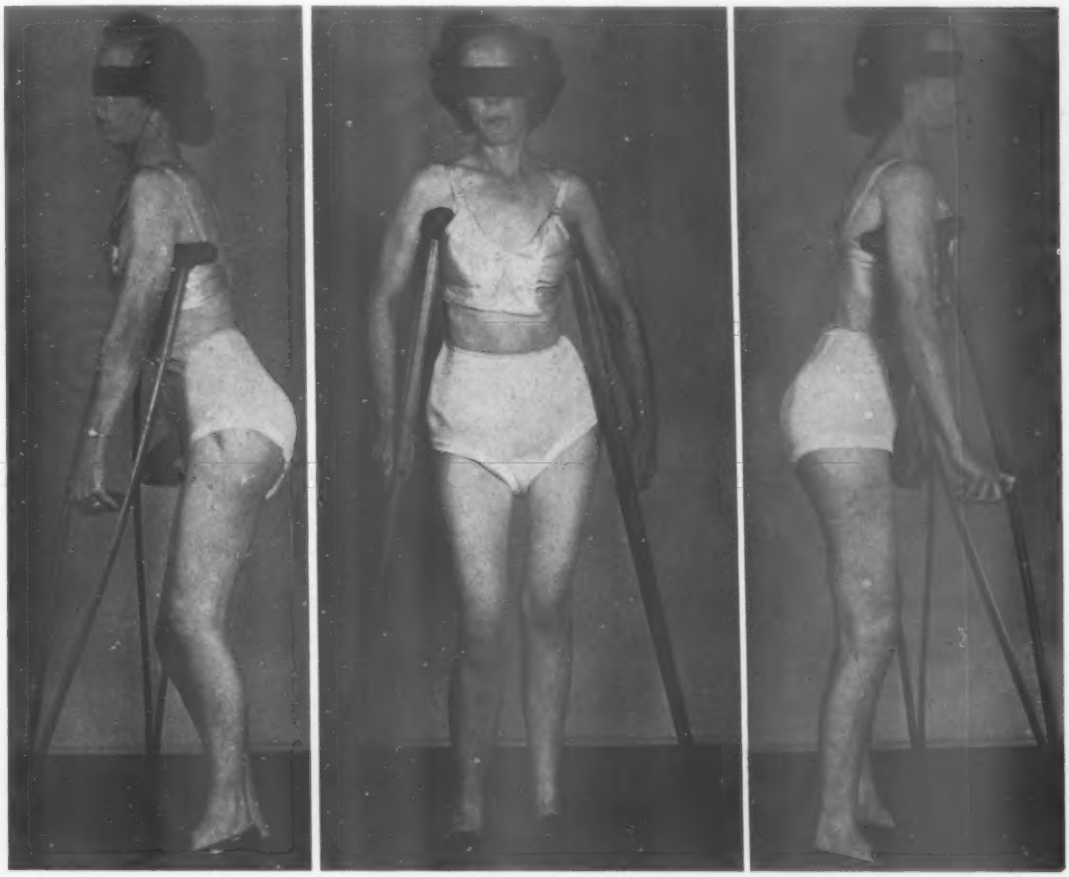

Fig. 9. Patient, October, 1948.

but sheds no light on the apparent cyclic or rhythmic shifts in the clinical pace of the disease. The latter episodes may be expected to occur in those tissues which abound in "susceptible histiocytes"; namely, the lymph nodes, lymphatic follicles, thymus, tonsils, liver, skin, bone marrow and even in the connective tissues of the heart, lungs and some endocrine glands. It may be that once an area is cleared of kerasin by the phagocytic ac- which raises the question of splenectomy for Gaucher's disease.

From the standpoint of the surgical risk, the older literature gives an operative mortality of about 20 per cent. More recent advances in surgery may be expected to lower this figure considerably. It is to be remarked that this patient withstood successively splenectomy (1934), tonsillectomy (1936) and a wide exposure of the left hip (1937). It is now quite generally agreed

FIG. 10. Same patient, October, 1948.

that splenectomy does not stop the progress of the disease or prevent bone involvement. Splenectomy does, however, relieve the patient of a burdensome spleen and, what is most important, stops the hemorrhagic tendency. In regard to the effect upon the osseous changes, Welt *et al.* pointed out that in Klercker's case, as well as in one of their own cases (Case 4) the osseous changes appeared soon after splenectomy. On the other hand, in another of their patients with the most extensive bone changes, the spleen had not been removed. The indication for splenectomy in these patients is therefore palliative but undoubtedly contributed largely to the subsequent comfort of the courageous patient reported in this paper (Fig. 9).

The most striking skeletal changes in this case evolved over a long period of time in the left femoral head. Since these followed upon a primary minimal pathological infiltration and pathological fracture, the residual alterations in the femoral head may be presumed to have occurred secondarily on the basis of an aseptic necrosis, weight-bearing stresses, and inadequate anatomical reduction and fixation of the fragments. The changes in the lumbopelvic areas which were not subjected to the same degrees of stress as the hip joint were less marked. The same may be said in degree regarding the supracotyloid portion of the ilium on the left side. The non-stress-bearing iliac wings were remarkably resistant to the disease and resolution here was almost complete. The changes in the lower lumbar vertebrae progressed very slowly over a period of about twelve years. The disc spaces between the last three lumbar vertebrae were definitely narrowed (Fig. 10). The subsequent and residual changes in the sacroiliac joints, which followed upon the more or less characteristic initial mottled appearance, resembled that which occurs there after infections; namely, juxta-articular increased density and tendency toward partial or complete obliteration of the joint space. As a further corollary to this may be mentioned the early "unhooking" at the symphysis on the right side; a sign not infrequently to be noted in infec-

FIG. 11. Same patient, right shoulder, October, 1948, some years after complaint of "rheumatism"; very little restriction of motion clinically.

tions of the sacroiliac bones and joints.

The extensive somewhat unusual changes noted in the right upper femur epitomized the lapse which may occur between an extensive skeletal lesion and clinical symptoms referable to that bone lesion. The opposite obtained in regard to her initial severe low back pain and sciatica and the long period of time which elapsed before there were any roentgenological changes to account for her symptoms. Similarly, some years had elapsed after the patient had first complained of "rheumatism" in both shoulders, before skeletal changes occurred (Fig. 11) on the roentgenogram. Since there is no apparent rule-of-thumb to be followed along this line, one should regard all symptoms relative to the skeletal system as suspect until proved otherwise. By the same token a known case of Gaucher's disease should have routine roentgenographic studies of the lumbopelvic areas at regular intervals.

Despite the rather clear-cut features of Gaucher's disease it is necessary to refer briefly to the differential diagnosis. Schein and Arkin emphasized, on the clinical side, that while the onset of osseous involvement in Gaucher's disease is often associated with intermittent pain in various bones and joints and low grade fever, the diagnosis can only be made by recognizing the underlying Gaucher's disease as well as the local condition. From the systemic or medical diagnostic angle as regards the splenomegaly, Bloem recommends the ruling out of leukemia, cirrhosis of the liver, hemolytic jaundice, splenic anemia, Banti's disease and thrombosis of the splenic vein. In regard to the related osseous changes, one has to consider among the more common lesions already mentioned, such more or less unusual diseases as multiple myeloma, chloroma, a certain peculiar anemia with sclerosis of the skeleton, some of the osteolytic bone tumors, Niemann-Pick's disease, some cases of amaurotic familial idiocy, Letterer-Siwe disease, Hand-Schüller-Christian disease and eosinophilic granuloma.

Lettere-Siwe disease occurs under two years of age, runs an acute or subacute course and is fatal in weeks or months. The destructive bone lesions occur chiefly in the skull.

Hand-Schüller-Christian disease often occurs between five and ten years of age. The osseous lesions occur chiefly in the optic or hypophyseal fossae and calvarium, which are responsible for the classic triad of symptoms: exophthalmus, diabetes insipidus and circumscript skull defects. The disease may lead to dwarfism and hypogonadism. It runs a chronic course of ten to fifteen years, death being usually due to secondary involvement of the hypothalamus or heart.

Eosinophilic granuloma arises in the marrow of one, a few or many bones. It is benign and may heal spontaneously or after simple removal. The presence of eosinophils is characteristic and thought to indicate an allergic origin.

Niemann-Pick disease is a malignant disease of infancy in which skeletal lesions are rare.

CONCLUSIONS

Osseous manifestations occur not infrequently in Gaucher's disease and add an important diagnostic criterion to the better known clinical signs and symptoms of this disease.

Bone lesions as noted on roentgenograms may be considered to be primary and secondary. The primary lesion is due to the actual infiltration of Gaucher's cells in the marrow. This may be manifested as a minimal, moderate or more extensive central translucent or osteolytic process. The ultimate complication on this basis is the pathological fracture. The secondary changes develop in the opposite direction toward condensation and are due to an aseptic necrosis upon which are superimposed the effects of mechanical stresses and weight bearing.

In the case herein reported the lumbopelvic structures and hip joints were affected in varying degrees, as was the right

shoulder joint. The lower lumbar vertebrae and their intervertebral discs were slowly and progressively affected over a long period of time in an osteoarthritic-like process. Evidence has been mentioned to show that the intervertebral discs do became involved in this disease at least secondarily to primary changes in the vertebral bodies.

The peculiar osteolytic and septate roentgenographic appearance of the right hip in this case is to be remarked.

The apparent reversibility of some of these osseous lesions has been mentioned.

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REFERENCES

1. ARKIN, A. M., and SCHEIN, A. J. Aseptic necrosis in Gaucher's disease. *J. Bone & Joint Surg.*, 1948, *30A*, 631–641.
2. BLOEM, T. F., GROEN, J., and POSTMA, C. Gaucher's disease. *Quart. J. Med.*, 1936, *5*, 517–527.
3. CUSHING, E. H., and STOUT, A. P. Gaucher's disease, with report of case showing bone disintegration and joint involvement. *Arch. Surg.*, 1926, *12*, 539–560.
4. JUNGHAGEN, S. Röntgenologische Skelettveränderungen bei Morbus Gaucher. *Acta radiol.*, 1926, *5*, 506–516.
5. MELAMED, S., and CHESTER, W. Osseous form of Gaucher's disease. *Arch. Int. Med.*, 1938, *61*, 798–807.
6. PHEMISTER, D. B. Changes in bones and joints resulting from interruption in circulation; nontraumatic lesions in adults with bone infarction; arthritis deformans. *Arch. Surg.*, 1940, *41*, 1455–1482.
7. PICK, L. Classification of diseases of lipoid metabolism and Gaucher's disease. *Am. J. M. Sc.*, 1933, *185*, 453–469.
8. POTTER, E. B., and MCRAE, C. C. Gaucher's disease: report of two cases, with remission in one following administration of liver extract. *Am. J. M. Sc.*, 1933, *185*, 92–96.
9. REISS, O., and KATO, K. Gaucher's disease; clinical study, with special reference to roentgenography of bones. *Am. J. Dis. Child.*, 1932, *43*, 365–386.
10. SCHEIN, A. J., and ARKIN, A. M. Hip-joint involvement in Gaucher's disease. *J. Bone & Joint Surg.*, 1942, *24*, 396–410.
11. WELT, S., ROSENTHAL, N., and OPPENHEIMER, B. S. Gaucher's splenomegaly, with especial reference to skeletal changes. *J.A.M.A.*, 1929, *92*, 637–644.

Vol. 63, No. 6

MULTIPLE MYELOMA*

AN ANALYSIS OF TWENTY-ONE PROVED CASES

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THIS paper is based on a study of all of the cases cross-indexed at the New York Hospital under the headings of multiple myeloma and its various synonyms in a fifteen year period between 1932 and 1947. There were only 21 definitely proved cases in this span of time. It is true that there were others with clinical, laboratory, and roentgenographic findings which warranted the acceptance of the same diagnosis, but only the 21 cases with positive microscopic proof from biopsy, sternal marrow puncture, or autopsy material were utilized in this analysis.

Ten of the cases are reported in some detail with illustrations of the important roentgenographic findings but the chief features of all 21 cases have been summarized in tabular form.

Although there has been considerable discussion and wide diversity of opinion regarding the nature of multiple myeloma and the origin of the predominant cells, Ewing's[4] designation of the disease as a specific malignant tumor, probably arising from a single cell type, is still the most acceptable conception. Later, in reviewing the classification of bone tumors, Ewing[5] limited the group of myelomas to those tumors arising from specific marrow cells. Wallgren[17] expresses a similar theory that all myelomas are made up of cells of the same fundamental types, showing, however, various stages of development, differentiation or degeneration. Geschickter and Copeland[7] designate the cells as plasma-like with an eccentric nucleus containing a spoke-like arrangement of chromatin. The cells themselves have been called lymphocytes, lymphoblasts, myelocytes, myeloblasts, erythroblasts and plasma cells. Wallgren suggests that because of atypical appearance of these plasma cells they be referred to as *myeloma* cells.

NATURE OF THE DISEASE

Multiple myeloma is a relatively uncommon but not rare type of malignant disease of bone which in its various forms shows resemblance to carcinoma, leukemia and lymphosarcoma. Ulrich[16] regarded multiple myeloma as a neoplastic disease midway between frank tumors and the leukemias. The usual site of origin is the bone marrow but occasionally extramedullary origin is encountered. Garland and Kennedy[6] define the disease as essentially a malignant tumor of bone marrow which may present itself in single or multiple foci and tends to involve notably the ribs, spine, skull, and pelvis. In later stages myelomatous deposits may appear in the liver, spleen, and lymph nodes. Bayrd and Heck[2] summarize their conception of the disease as caused by a single cell type arising from the reticuloendothelial system in a dysplastic cell line. They regard multiple myeloma uniformly malignant and usually rapidly fatal. Batts[1] who reported 40 cases in 298,546 hospital admissions found an average duration of two and one-half years with fatal termination after the diagnosis had been made. He found osseous changes recognizable roentgenographically in 60 per cent of his cases, and autopsy revealed involvement of liver, spleen, kidneys and the nervous system in many cases. Ghormley *et al.*[10,11] reviewed 127 cases and concluded that multiple myeloma is a highly malignant tumor of bone marrow which tends to occur after the fifth decade. Histopathologically, they point out the predominance of cells closely resembling plasma cells, now usually referred to as myeloma cells. They found wide variation in degree of skeletal involvement, ranging from no demonstrable bone changes to extensive bone destruction.

The disease has been referred to in the literature as plasmacytoma, plasmoma,

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erythroblastoma, myelocytoma, plasma cell myeloma and plasmacytic leukemia. The existence of the latter as a distinct entity seems highly doubtful but there is recognized a leukemic phase of the disease.

SOLITARY FORM OF MYELOMA

This form of myeloma is extremely rare or possibly not a separate entity but merely an early phase of the disease. Toth and Wintermantel[15] reviewed the cases of so-called solitary myeloma and found that the majority become generalized in time. Gootnick[9] reported 2 cases of solitary myeloma and reviewed 59 other cases from the literature. His conclusions were: (1) The lesion may be solitary in the beginning, later becoming generalized. (2) The solitary lesion may be benign, remaining localized throughout its course. Gootnick also described the roentgen appearance of solitary myeloma as having two forms, one a cystic and trabeculated lesion, closely resembling a fat cell tumor, the other a purely destructive osteolytic lesion quite similar to metastatic cancer.

Geschickter[8] reported one case of solitary myeloma and pointed out the resemblance of the lesion to metastatic carcinoma and bone cyst.

Paul and Pohle[14] reported 5 cases of solitary myeloma and considered this form of the disease as unusual but not rare. They believe that the degree of malignancy varies, ranging from a benign form with localization to early generalization (typical multiple myeloma). They also described two main forms of solitary myeloma, one resembling a giant cell tumor with trabeculated, multicystic appearance, the other essentially osteolytic in character.

Bayrd and Heck[2] regard the distinction between solitary and generalized myeloma as artificial since it seems likely that the existence of a solitary bone lesion is merely a phase in the same disease. There is also considerable doubt that solitary myelomas can ever be benign since in many instances they have become generalized in a later stage. Two cases in our series showed solitary lesions in the initial examinations (Cases II and V). However, one of these (Case V) later developed multiple foci.

CLINICAL FEATURES

Multiple myeloma has no characteristic symptoms of onset and no definite early clinical picture.

Pain. This is probably the most constant feature in the symptomatology. Bayrd and Heck encountered pain, usually in the lower back, in 86 per cent of their cases. The pain may be vague, intermittent, severe, or wandering. Levitt and Levy[13] report a case of a male, aged twenty-five, who had a dull ache in his back and thighs, more or less continuously for two years before there was a change to severe pain which led to the recognition of multiple myeloma. In the series being considered in this review, pain was a presenting symptom in 18 cases.

Fractures. There is considerable variation in incidence. Bayrd and Heck report 16 per cent not including compressions of vertebral bodies, whereas the figures of Geschickter and Copeland[7] show an incidence of 62 per cent of pathologic fractures with the ribs being most frequently involved. Of the cases in our series 4 showed pathological fractures.

Tumor. Batts found palpable tumors in one-half of his cases, Bayrd and Heck in only 12 per cent. Six of our cases had palpable tumors.

Other Clinical Features.

(1) Cachexia.

(2) Profound anemia.

(3) Albuminuria.

(4) Presence of Bence-Jones protein, ranging from 8 to 65 per cent positive in various series. Bence-Jones protein was found in 7 cases in our series.

(5) Protein concentration is often elevated. It has been pointed out that a level of 8.0 gm. in the protein determination is rarely encountered in any other disease than multiple myeloma.

(6) Albumin-globulin ratio is usually reversed.

(7) Elevation of blood calcium is com-

mon, serum phosphorus usually normal or nearly so.

(8) Nephrosis with non-protein nitrogen retention due to obstructive effect of tubular casts of the Bence-Jones protein.

(9) Chronic bronchitis and emphysema.

(10) Neurologic symptoms and signs related to extent and location of destructive bone lesions.

ROENTGEN CHARACTERISTICS

Roentgen findings in multiple myeloma are widely varied. In at least one case of the group studied there were no recognizable changes whatsoever; in several there was only a diffuse generalized demineralization hardly to be distinguished from the senile or postmenopausal types of osteoporosis, and very often accompanied by compression of vertebral bodies. At times the demineralization is of an uneven, spotty type creating a granular or stippled effect, especially notable in the ribs, skull or pelvis. A peculiar criss-cross or honeycomb effect in the trabecular structure of the proximal portions of the shafts of the femurs and humerus was encountered in several instances. This "lattice" effect is accentuated against the background of the radiolucent medulla.

Osteolytic lesions also vary considerably in number, size, locality and structural appearance. Many of the so-called "solitary" forms or isolated lesions have a cystic and trabeculated character, not unlike giant cell tumors or if there is considerable expansion with destructive element, resemble osteochondrosarcoma.

The most typical form of the disease in bones is the familiar widespread, sharply demarcated or "punched-out" osteolytic lesion so strongly suggestive of the disease, especially in the skull or ribs.

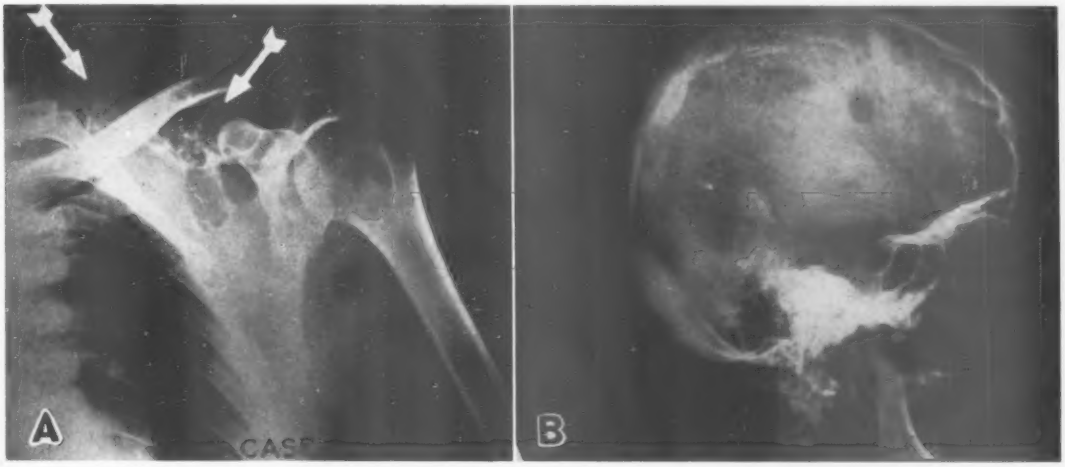

Fig. 1. Case 1. (*A*) Left shoulder: Destructive lesion, upper half of scapula with a large soft tissue mass containing irregular calcification (osteolytic lesion resembling osteochondrosarcoma). (*B*) Multiple punched-out, radiolucent areas.

CASE REPORTS

Case 1 (No. 473380). L. B., Columbian male, aged forty-three, admitted to New York Hospital March 31, 1947, with a history of aching pain in the left shoulder following a fall twenty months previously. A swelling appeared two to three weeks later and this increased gradually in size until the time of admission. No other complaints. The past history was negative except for a positive serological test for syphilis in January, 1947.

Physical Examination. There was a large, hard, only slightly tender mass in the left scapular region. It measured about 12 cm. in diameter with about 4 cm. elevation.

Laboratory Findings. Urine: protein one to two plus. Test for Bence-Jones protein, consistently negative. Blood: hemoglobin, 13 gm.;

red blood cell count, 4.2 million; white blood cell count, 8,000. Serology: Wassermann reaction, positive; albumin-globulin ratio, 5.6:2.3; acid phosphatase, 1.1 mg.; calcium, 8.7 mg.

Roentgen Findings. Left shoulder: Destructive lesion involving upper half of scapula with a large soft tissue mass containing calcifications. This resembled an osteochondrosarcoma in appearance. Skull: Multiple punched-out radiolucent areas typical of multiple myeloma (Fig. 1).

Pathology. Biopsy of left shoulder tumor showed it composed of cells identical in appearance with plasma cells. Careful search revealed no mitotic figures. Sternal marrow aspiration: Total count 75,000 cells with 72 per cent myeloma cells.

Course. Treated with intravenous stilbamadine in individual doses of 150 mg. to a total of 2.25 gm. Pain in shoulder disappeared under treatment. Discharged to care of local doctor in Columbia, S. A., with no further follow-up.

CASE II (No. 472061). M. A., male, aged fifty-nine, was admitted to New York Hospital April 2, 1947, complaining of pain in the low back and left hip for five months. This pain was severe and usually of an aching character accentuated by movement. He lost about 20 pounds in the five month interval.

Physical Examination. Tenderness to pressure over lumbosacral region posteriorly. There were no other significant findings. The neurological examination was negative.

Laboratory Findings. Urine, negative. Blood: hemoglobin, 11.8 gm.; red blood cell count, 3.3 million. Serology: calcium, 9 mg.; protein, 9.8 mg.; albumin-globulin ratio, 4.7:5.1; phosphorus, 3.9 mg.; alkaline phosphatase, 3.0 mg.; acid phosphatase, 0.7 mg.

Roentgen Findings. An extensive examination including spine, pelvis, ribs and skull showed a solitary osteolytic lesion involving the fifth lumbar vertebra with no other bone changes. This was regarded as probable metastatic neoplasm (Fig. 2).

Pathology. A bone marrow aspiration showed definitely abnormal clumps of plasma cells indicating multiple myeloma.

Course. The patient was treated with stilbamadine. He received a total of 1.53 grams while in the hospital and was discharged on the fortieth day, improved. He was followed up in the clinic and continued to show improvement but developed a compression fracture of the eleventh dorsal vertebra eight months later. This patient is still living.

FIG. 2. Case II. Lumbar spine: Solitary osteolytic lesion of L5.

CASE III (No. 449141). G. A., Peruvian male, aged fifty-nine, admitted to New York Hospital July 2, 1946, with a history of anemia and diarrhea plus progressive weakness and vague generalized muscle pain. The diarrhea dated back to about eight years before admission and sometime later he was told by his physician that he had colitis. One year before admission his condition was diagnosed as a case of sprue. A few months prior to admission he developed rather marked weakness with attacks of vertigo, numbness of the hands and arms, muscle pains and intermittent tinnitus. He lost 25 pounds in weight over the eight year period.

Physical Examination. Evidence of moderate chronic weight loss with no other significant findings except slight abdominal distention.

Clinical Impression on Admission. Sprue.

Laboratory Findings. Blood: hemoglobin, 12.2 gm.; red blood cell count, 4.2 million; white blood cell count, 6,600. Blood chemistry: protein, 9.4 mg.; albumin-globulin ratio, 3.6:5.8; serum calcium, 9 mg.; phosphorus, 2.9 mg.; phosphatase, 3 mg.; urine, one plus albumin; Bence-Jones protein, positive.

Roentgen Findings. Diagnosis of multiple myeloma based on granular appearance of skull, mandible and ribs, plus rarefaction and

Fig. 3. Case III. (*A*) Skull: Lateral view showing granular appearance with no localized punched-out areas of radiolucency. (*B*) Pelvis: Anteroposterior view shows slight demineralization, particularly in upper ends of femora. (*C*) Humeri show rarefaction and prominent interlacing trabeculation, or "lattice" effect. (*D*) Femora: These show changes similar to those in the humeri; the "lattice" effect is more prominent.

prominent interlacing trabeculation in femora and humeri.

All other roentgenograms, including a gastrointestinal examination with small intestinal studies, were negative. There was no evidence of sprue.

Sternal marrow puncture revealed 56,000 nucleated cells with 26 per cent plasma cells.

Course. When the diagnosis of multiple myeloma was established, the patient was discharged to the care of his physician in Peru. There has been no further follow-up.

Case IV (No. 158576). L. B., male, aged sixty-four, admitted to New York Hospital, November 25, 1942, with a history of low back pain for seven months. Shortly before admission a mass appeared over the right sacroiliac region. This was biopsied before admission. The past history was non-contributory.

Physical Examination. Negative except for a hard palpable mass in the right sacroiliac region. This measured about 10 cm. in diameter and it was tender. The patient was pale and appeared chronically ill.

Laboratory Findings. Urine, negative. Bence-Jones protein, negative. Blood: hemoglobin, 10 gm.; red blood cell count, 3.6 million; white blood cell count, 9,200; serum phosphorus, 2.22 mg.; serum phosphatase, 4.45 mg.; total

serum protein, 8.8 mg.

Biopsy. Plasma cell myeloma.

Roentgen Findings. Extensive typical punched-out radiolucent areas in skull, entire spine, pelvis, ribs and right shoulder (Fig. 4).

Course. The patient received extensive roentgen therapy with definite relief of pain. On the day of discharge, December 22, 1947, he fractured his left humerus while turning in bed. He was allowed home with a splint. There has been no further follow-up.

CASE V (No. 425142). I. W., a white, German born female, aged fifty-one, was admitted to New York Hospital, September 20, 1946, complaining of a swollen, painful, left knee for five months. Five months before admission, without trauma or previous infection, the patient developed a dull constant aching pain which gradually increased in severity. About one month before admission, the knee became swollen and slightly reddened. She then began to have night sweats, general malaise, and weakness with a 5 to 10 pound weight loss.

Past History. Negative except for treated syphilis.

Physical Examination. The left knee was diffusely swollen, reddened, warm to touch and extremely tender over the medial aspect. There was no evidence of joint fluid. The motion was limited. The heart was enlarged and the liver and spleen were palpable and non-tender.

Roentgen Findings. Complete skeleton: The left knee showed a rather large osteolytic lesion in the distal end of the femur involving the median epicondyle. There was complete loss of osseous detail and expansion of thinned cortex, but no definite cortical break and no periosteal reaction. There were also suspicious ill defined osteolytic areas in the right greater trochanter, neck of the left femur, and neck of left scapula. The skull was not examined until later when it showed small areas of involvement in the frontal bone. The original roentgenologic impression was osteolytic metastatic bone disease.

Pathology. Sternal marrow puncture was negative, but biopsy of the tumor of the left femur showed a myeloid myeloma.

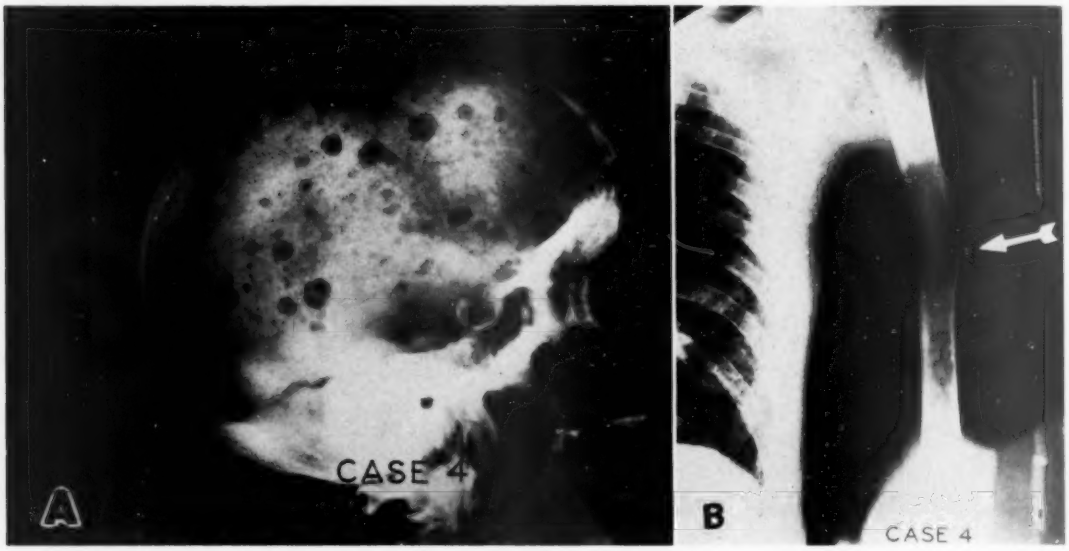

FIG. 4. Case IV. (*A*) Skull: Lateral view shows typical, multiple, punched-out, radiolucent areas. (*B*) Left humerus: Extensive, destructive, osteolytic lesion with a pathologic fracture of the mid-shaft.

Laboratory Findings. Urine—negative. No Bence-Jones protein. Blood count and blood chemistry normal except for slight anemia (3.5 million).

Course. This patient has been treated extensively with roentgen therapy (both knees, hips, pelvis, cervical spine and upper dorsal spine) with some relief. Last visit was on March 10, 1948.

CASE VI (No. 37029). W. G., white male, aged sixty-one, was admitted to New York Hospital, August 4, 1947, complaining of severe steady pain at the base of the spine for two

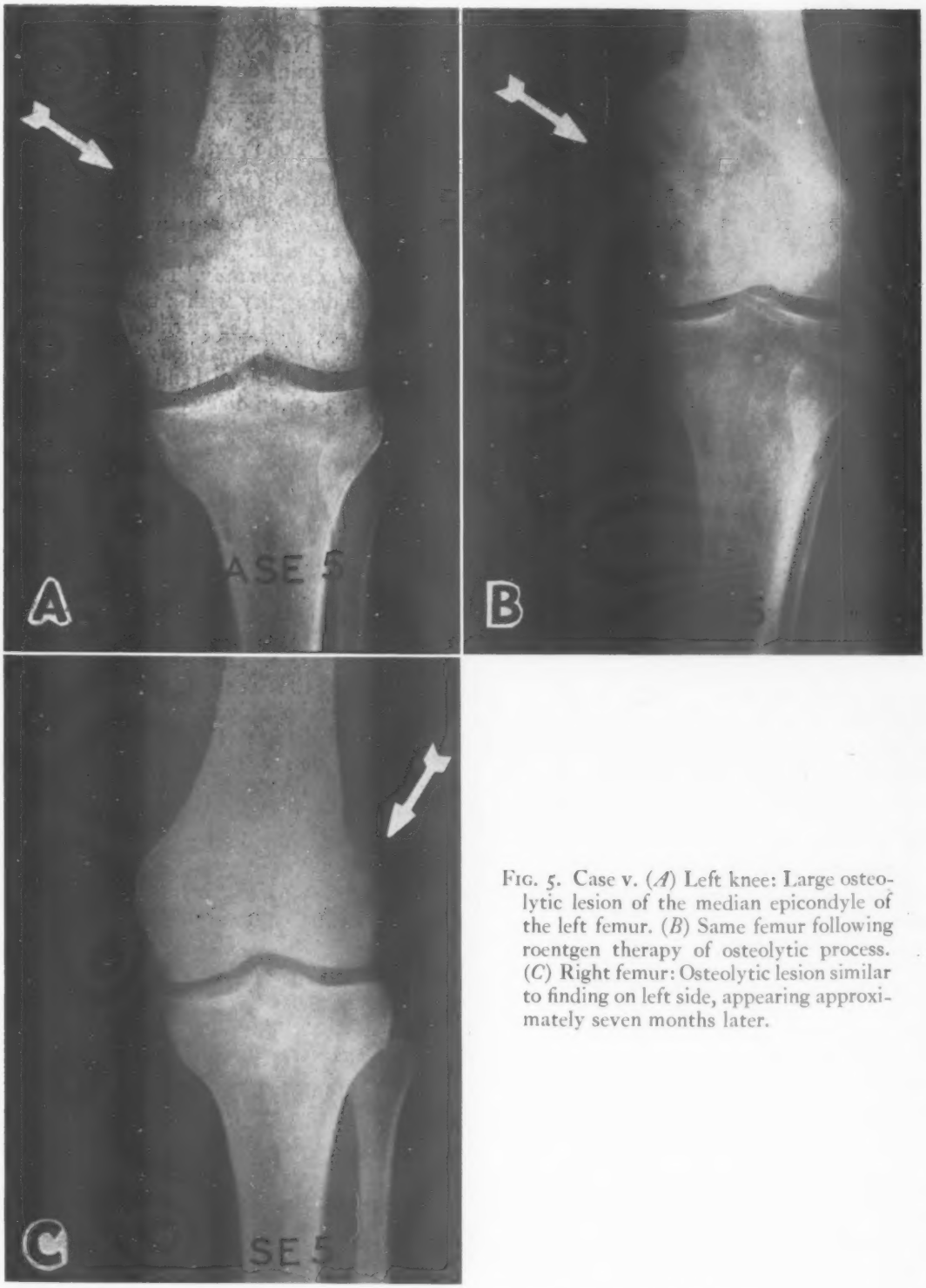

Fig. 5. Case v. (*A*) Left knee: Large osteolytic lesion of the median epicondyle of the left femur. (*B*) Same femur following roentgen therapy of osteolytic process. (*C*) Right femur: Osteolytic lesion similar to finding on left side, appearing approximately seven months later.

months. This was accentuated by any movement, especially walking. His gait became waddling. Codeine and aspirin gave no relief. The patient had lost 20 pounds in weight in the five years prior to admission.

Past History. Non-contributory except for poor appetite during the past two years. Examination one month previously at another

FIG. 6. Case VI. Skull: Lateral view shows multiple, punched-out, radiolucent areas.

hospital showed a possible carcinoma of the stomach.

Physical Examination. There were no significant findings except for severe pain over the lower sacrum on flexion or extension of the back.

Roentgen Findings. A gastrointestinal series showed no evidence of gastric neoplasm. There was an antral gastritis and prolapse of the gastric mucosa into the base of the duodenal bulb. Roentgenograms of the lumbar spine and pelvis showed some slight generalized demineralization with very faint, ill defined, punched-out, radiolucent areas. This finding was indefinite but it suggested the possibility of multiple myeloma and skull films were requested. These showed a definite moth-eaten appearance with small, punched-out, radiolucent areas involving the entire skull.

Laboratory Findings. Urine: trace of albumin. Six specimens negative for Bence-Jones protein (five tests positive on second admission three months later). Blood: hemoglobin, 12.5 gm.; red blood cell count, 3.4 million; protein, 9.1 mg.; albumin-globulin ratio, 3.2:5.9; phosphorus, 4.6 mg.; acid phosphatase, 0.54 mg.; alkaline phosphatase, 2.6 mg.

Sternal marrow aspiration on August 10, 1947, showed a total count of 30,000, with 71 per cent myeloma cells.

Course. The patient was treated with stilbamadine with diminution of back pain.

CASE VII (No. 104698). A. T., male, aged fifty-eight, Czechoslovakian born tailor, was admitted to New York Hospital, August 19, 1935, complaining of severe dull throbbing pain in the low back since March, 1931. The onset was sudden and he was incapacitated for the next month. Following this he gradually developed transitory, migratory pains in the chest, shoulders, arms and legs. These symptoms became more persistent and severe with the passage of time.

Physical Examination. There was evidence of lumbar deformity with a tilted pelvis and a waddling gait and the sternum was unusually prominent. There was bony enlargement or prominence at the medial end of the left clavicle measuring 3 cm. in diameter. This was painful.

Laboratory Findings. Urine: albumin, negative. Bence-Jones protein, absent. Blood: red blood cell count, 3.2 million; hemoglobin, 55 per cent; calcium, 10.4 mg.; serum phosphatase, 3.8 mg.; serum albumin, 3.3 mg.; serum globulin, 4.1 mg.

Roentgen Findings. The spine, thoracic cage, pelvis, long bones and skull all showed extensive demineralization and multiple punched-out, radiolucent areas. These findings were interpreted at the time as either a multiple myeloma or some metabolic dysfunction such as hyperparathyroid disease (Fig. 7).

Bone Marrow Biopsy. (September 4, 1935) Plasma cell myeloma. (Previous biopsy on August 1, 1932, at Monmouth Memorial Hospital showed multiple myeloma—biopsy of lumbar spine.)

Course. The patient was treated by roentgen therapy with little improvement. He eventually had pathological fractures of the femur and humerus. He died on July 5, 1936.

CASE VIII (No. 374350). M. L., male, aged fifty-seven, admitted to New York Hospital on December 2, 1943, complaining of severe low back pain for four months. This became so severe that he could hardly move without excruciating pain and could sometimes hardly turn in bed. He lost 15 pounds in the four months interval. He had frequent vomiting in the last six weeks before admission.

Past History. Non-contributory.

Physical Examination. There was tenderness on pressure over the posterior spines of D2 and D3. A neurological examination showed vibration sense diminished to absent and muscle pain and tendon pain diminished in the left leg. The reflexes were normal.

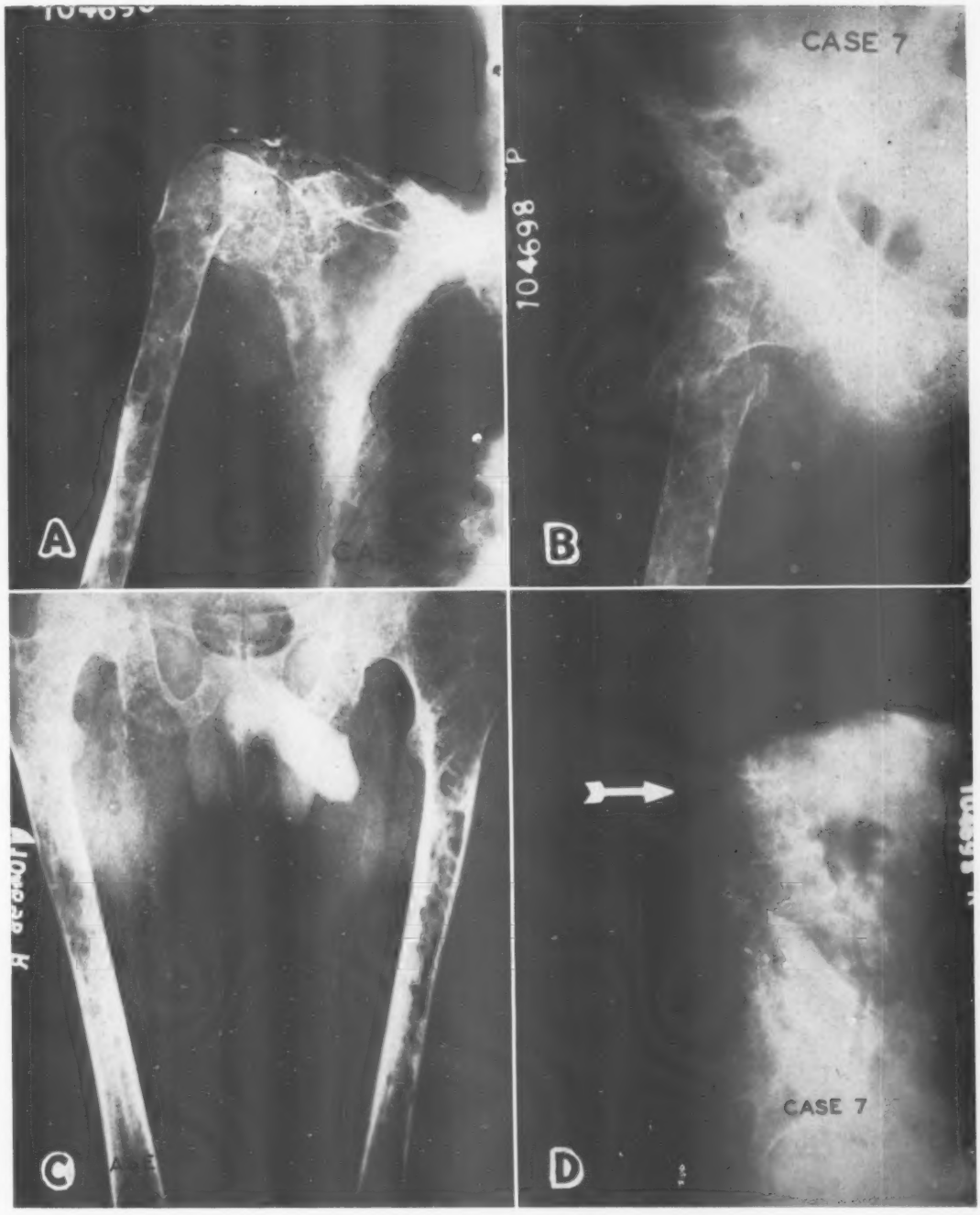

Fig. 7. Case vii. (*A*) Extensive punched-out, radiolucent, or osteolytic lesions with a pathological fracture of the upper end of the humeral shaft. (*B*) Right upper femur: Extensive osteolytic lesions with a pathological fracture of the upper shaft. (*C*) Femoral shafts: Extensive, osteolytic lesions. This case also demonstrates criss-cross trabeculations. (*D*) Lumbar spine: Lateral view shows extensive osteolytic involvement with complete collapse of the first lumbar vertebra.

Laboratory Findings. Urine: four plus albumin. Bence-Jones, negative. Blood count: hemoglobin, 7.5 gm.; red blood cell count, 2.7 million (1.5 million on discharge); albumin, 5.4 mg.; globulin, 3.6 mg.; acid phosphatase, 0.4 mg.

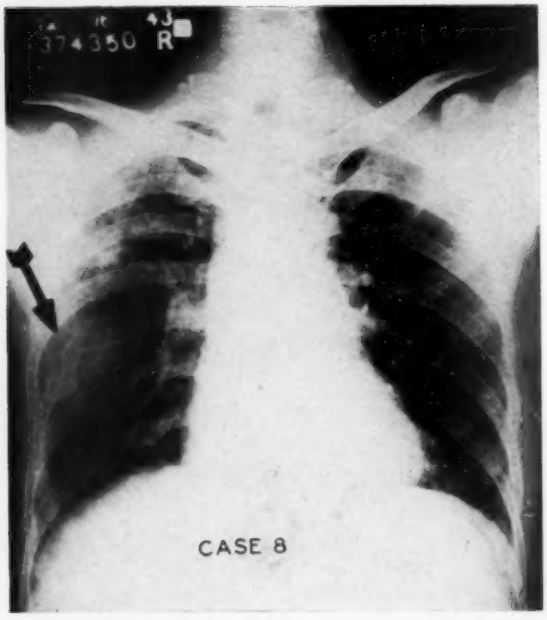

FIG. 8. Case VIII. Chest: Posteroanterior view shows generalized rib destruction with circumscribed areas of radiolucency and a tumor of the right seventh rib.

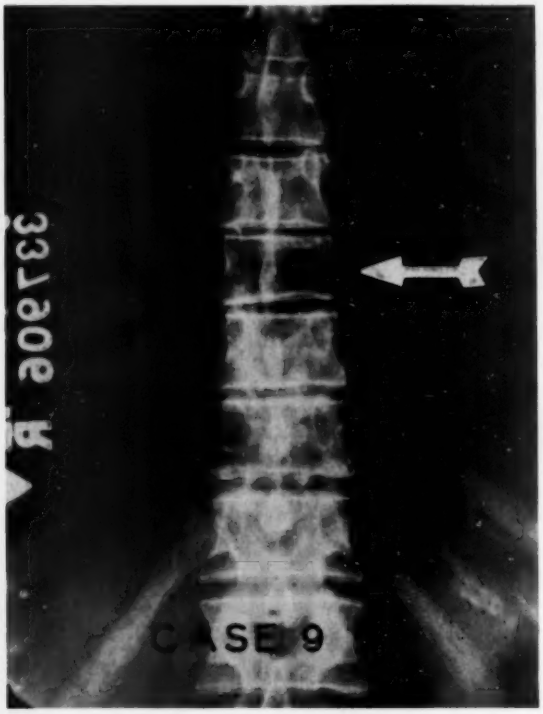

FIG. 9. Case IX. Dorsal spine: Anteroposterior view shows a destructive lesion of D9 with slight left-sided wedge.

Roentgen Examinations. The skull was normal. The chest showed generalized rib demineralization and many well circumscribed areas of radiolucency. The right seventh rib posteriorly showed an area of local expansion 6 cm. long with an associated soft tissue mass. There was a small area of local rib expansion involving the left ninth rib in the posterior axillary line. A roentgenogram of the spine and pelvis showed multiple punched-out areas of radiolucency and a compression fracture of D12.

Pathology. Biopsy of the right seventh rib on December 30, 1943, was reported multiple myeloma, "plasma cell" type.

FIG. 10. Case X. Femurs: Multiple large and small osteolytic lesions.

Course. The patient was treated with roentgen therapy and transfusion. He did not improve and died on the forty-fourth hospital day, less than six months after the onset of symptoms.

CASE IX (No. 337906). P. V., male, aged fifty-six, was admitted to New York Hospital, September 11, 1942, with a history of severe back pain for three or four months. This followed a strain of his back. It was treated by a local physician with a plaster which gave no

relief. Five weeks before admission he developed pain in the left knee. This subsided after two weeks of rest. The back pain became increasingly severe.

Physical Examination. Slight upper dorsal kyphosis with pressure tenderness over D9. Flexion and extension was limited, with pain in dorsal region on active or passive motion. There were no other findings. The extremities were negative.

Laboratory Findings. Urine: albumin four plus. Bence-Jones test doubtful positive. Blood: hemoglobin, 7.5 gm.; red blood cell count, 3.2 million; total protein, 7.8 mg.; serum calcium, 10.2 mg.

Roentgen Examination. The skull was negative. The dorsal spine showed an osteolytic lesion of D9 with almost complete loss of normal trabecular structure and slight left-sided wedging deformity. The lumbar spine and pelvis showed no definite osteolytic areas but there was a generalized bone demineralization with ill defined areas of radiolucency and loss of normal trabecular structure.

Pathology. Sternal marrow aspiration, on September 20, 1942, showed plasma cell myeloma.

Course. The patient was given roentgen therapy with some relief of pain. Dorsal and lumbar posterior fields were treated. On May 28, 1943, a roentgenogram of the right knee showed an osteolytic lesion in the medial condyle. This was also treated, with relief of pain and reduction of swelling.

The patient was later admitted to Bellevue Hospital. He died in December, 1943, about eighteen months after the onset of symptoms.

Case x (No. 188567). K. W., a white female, widow, aged fifty-four, was admitted to the New York Hospital with a history of pain in chest, back and hips for three weeks.

Present Illness. The patient had a productive cough with occasional chest pain for three or four years. One year before admission she fractured her right clavicle lifting a mattress. This apparently healed but four months later she refractured the same clavicle in a bus accident. During the last eight months before admission she was easily fatigued, her cough increased and in the three weeks before admission she developed pain in her chest, sternum, low back and hips. She lost 35 pounds in weight in a few months.

Physical Examination. There was evidence of weight loss but no other significant physical findings. The patient complained of pain but there were no definite localized areas of tenderness.

Laboratory Findings. Urine: specific gravity, 1.010 to 1.030; two plus albumin on numerous occasions. Bence-Jones test, repeatedly negative. Blood: hemoglobin, 64 per cent; red blood cell count, 2.9 million; white blood cell count, normal. Chemistry: serum protein, 9.1 mg.; albumin-globulin ratio, 1.8:7.3; serum calcium, 10.4 mg.; phosphorus, 4.9 mg.; serum phosphatase, 3.5 mg.

Other laboratory examinations, including serology, sedimentation rate, platelet count, clotting time, bleeding time, urea clearance test, sputum cultures, basal metabolic rate and bronchoscopy were negative or normal.

Roentgen Findings. Roentgenograms of the chest showed an old healed fracture of the right clavicle. There were also osteolytic lesions of three ribs (right fifth, sixth and eleventh) and a collapsed ninth dorsal vertebra. Examination of the skull and long bones showed multiple large and small osteolytic areas in the cranial vault and most of the long bones. These were interpreted as either extensive osteolytic metastases or multiple myeloma.

Biopsy. A section removed from the tibia on September 3, 1938, was diagnosed plasma cell myeloma.

Course. The patient was given a course of roentgen therapy (irradiation to anterior and posterior torso) with some relief of pain, but her general condition became progressively worse and she was discharged on the sixty-eighth hospital day to a nursing home for terminal care.

SUMMARY AND CONCLUSIONS

1. Twenty-one proved cases of multiple myeloma have been reviewed and ten of these are reported in some detail.

2. Wide variation in the roentgenographic appearance of the osseous structures was encountered. Two cases in the series showed no recognizable change whatever, two showed only a diffuse osteoporosis, hardly to be distinguished from hyperparathyroidism or the senile type of demineralization. The other cases had changes in the bones which ranged from "suggestive" to "characteristic." The multiple,

TABLE I

THE CASE Nº	PATIENTS PRESENTING COMPLAINT	ROENTGEN OSSEOUS CHANGES	PATH. FRACTURE	TUMOR	MANNER OF DIAGNOSIS
1	PAIN AND SWELLING LEFT SHOULDER	TUMOR LFT. SCAPULA TYPICAL SKULL LESIONS	NO	YES	TUMOR BIOPSY ST. PUNCTURE
2	PAIN LOW BACK AND RIGHT HIP	SOLITARY OSTEOLYTIC LESION 5th LUMBAR	NO	NO	BONE MARROW ASPIRATION
3	PROGRESSIVE WEAKNESS. VAGUE PAIN	GRANULAR SKULL + RIBS HONEYCOMBED FEMORA	NO	NO	STERNAL PUNCTURE
4	LOW BACK PAIN	TYPICAL WIDESPREAD INCLUDING SKULL	YES	YES	TUMOR BIOPSY
5	PAIN + SWELLING LEFT KNEE	LARGE OSTEOLYTIC LESION OF FEMUR	NO	YES	TUMOR BIOPSY
6	LOW BACK PAIN	GEN. DEMINERALIZAT'N TYPICAL SKULL	NO	NO	STERNAL PUNCTURE
7	LOW BACK PAIN	TYPICAL WIDE SPREAD · FAR ADVANCED	YES	NO	BONE MARROW BIOPSY
8	SEVERE BACK PAIN (D-12 → L-2)	TYPICAL RIBS, SPINE AND PELVIS	NO	YES	RIB BIOPSY
9	MID DORSAL BACK PAIN	OSTEOLYTIC LESIONS D-9 + RT. FEMUR	NO	NO	STERNAL PUNCTURE
10	PAIN CHEST BACK AND HIPS	TYPICAL LESIONS SKULL + LONG BONES	YES	NO	BIOPSY OF TIBIA
11	DULL LOW BACK + GEN. BONE PAIN	TYPICAL SKULL, RIBS, SPINE + FEMORA	NO	YES	BIOPSY AUTOPSY
12	CRAMPS + NUMBNESS OF FINGERS	TYPICAL RIBS, SPINE AND PELVIS	NO	NO	AUTOPSY
13	ACHING PAIN RT. LOW BACK	NONE	NO	NO	ST. PUNCT. AUTOPSY
14	PROGRESSIVE EMACIATION + BACK PAIN	GENERALIZED BONE DEMINERALIZATION	NO	NO	AUTOPSY
15	BACK PAIN HEIGHT DECREASE	TYPICAL WIDE SPREAD LESIONS	YES	YES	AUTOPSY
16	FREQUENT HEADACHE + WEAKNESS	GEN. DEMINERALIZATION. TYPICAL SKULL	NO	NO	STERNAL PUNCTURE
17	BACK PAIN	TYPICAL SKULL, SPINE, PELVIS, HUMERI + FEMORA	NO	NO	BIOPSY AUTOPSY
18	LOW BACK PAIN	GEN. DEMINERALIZATION. TYPICAL SKULL	NO	NO	STERNAL PUNCTURE
19	WEAKNESS + DULL LOW NECK PAIN	GEN. DEMINERALIZAT'N. TYPICAL LESION D. SPINE	NO	NO	AUTOPSY
20	SEVERE LOW BACK PAIN	GEN. DEMINERALIZATION. TYPICAL SKULL.	NO	NO	STERNAL PUNCTURE
21	FATIGUE, DYSPNOEA NUMBNESS FINGERS	SPOTTY DEMINERALIZAT'N QUESTIONABLE SKULL	NO	NO	STERNAL PUNCTURE

punched out lesions of the skull, ribs, and pelvis were present in fourteen cases. These, however, at times closely resembled osteolytic metastases of carcinoma, especially of the breast. Therefore, it is felt that there is no pathognomonic roentgenologic sign or lesion in multiple myeloma.

3. The possibility of myeloma in a solitary form is considered and the eventual behavior of "solitary" lesions in our own

Table II

THE CASE Nº	THE HOSPITAL NUMBER	PT'S SEX AGE	DURATION SYMPT	BENCE JONES PROT.	URINE ALBUMIN	TOTAL SERUM PROT.	ALB. GLOB. RATIO	R.B.C. MILLIONS	TOTAL SERUM CALC.
1	473380	♂43	20 mo.	NEG	2+	8.1	5.7/2.4	4.2	8.7
2	472061	♂59	5 mo.	NEG	0	9.8	4.7/5.1	3.3	9
3	449141	♂59	INDEFINITE	POS.	3+	9.4	3.6/5.8	4.6	9
4	158576	♂64	7 mo.	NEG	0	8.8	NOT DONE	3.6	NOT DONE
5	425142	♀50	5 mo.	NEG	0	7.3	5.0/2.3	3.5	9
6	37029	♂61	2 mo.	POS	3+	10.3	3.2/5.9	2.9	9.6
7	104698	♂58	4 yr.	NEG	0	7.8	3.8/4.0	3.2	11.0
8	374350	♂57	2 yr.	NEG	4+	9.0	5.4/3.6	2.7	NOT DONE
9	337906	♂56	4 mo.	NEG	3+	7.8	NOT DONE	3.0	10.2
10	188567	♀53	3 wk.	NEG	3+	9.6	1.8/7.3	2.8	10.4
11	90923	♀47	3 yr.	POS	1+	3.7	3.1/0.6	2.1	9
12	240584	♂38	14 mo.	NEG	4+	9.5	2.2/7.3	2.0	14.8
13	319875	♀63	3 yr.	POS	4+	4.6	NOT DONE	3.2	NOT DONE
14	340528	♂63	2 yr.	POS	3+	6.7	5.2/1.5	1.9	10.4
15	374274	♀72	3 yr.	POS	1+	6.4	4.5/1.9	2.9	13.4
16	421048	♀59	1 yr.	NEG	1+	10.4	3.0/7.4	2.5	11.0
17	442402	♂61	3 wk.	POS	4+	7.5	5.6/1.4	1.9	10.7
18	449134	♂63	8 mo.	NEG	0	7.9	5.3/2.6	3.5	9.3
19	467763	♂71	2 mo.	NOT DONE	1+	NOT DONE	NOT DONE	3.6	NOT DONE
20	491344	♂61	2 mo.	NEG	1+	11.6	3.0/8.6	2.2	10.9
21	410290	♂58	1 yr.	NEG	1+	15.2	4.2/11.0	2.4	NOT DONE

series and those reported in the literature. It seems quite definite that most of these later become generalized. There is considerable doubt at this time that the disease is ever present in a benign form.

4. The outstanding symptoms and laboratory findings in this series have been presented in table form (Tables I and II).

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REFERENCES

1. BATTS, M., JR. Multiple myeloma. *Arch. Surg.*, 1939, *39*, 807–823.
2. BAYRD, E. D., and HECK, F. J. Multiple myeloma. *J.A.M.A.*, 1947, *133*, 147–157.
3. EHRLICH, D. R. Multiple myeloma. *Radiology*, 1934, *23*, 418–428.
4. EWING, J. Neoplastic Diseases: A Treatise on Tumors. Fourth edition. W. B. Saunders Company, Philadelphia, 1940, pp. 321–327.
5. EWING, J. Review of classification of bone tumors. *Surg., Gynec. & Obst.*, 1939, *68*, 971–976.
6. GARLAND, L. H., and KENNEDY, B. R. Roentgen treatment of multiple myeloma. *Radiology*, 1948, *50*, 297–317.
7. GESCHICKTER, C. F., and COPELAND, M. M. Tumors of Bone. Revised edition. American Journal of Cancer, New York, 1936, p. 448.
8. GESCHICKTER, C. F. Multiple myeloma as single lesion. *Ann. Surg.*, 1930, *92*, 425–433.
9. GOOTNICK, L. I. Solitary myeloma. *Radiology*, 1945, *45*, 385–391.
10. GHORMLEY, R. K., and POLLOCK, G. A. Multiple myeloma. *Surg., Gynec. & Obst.*, 1939, *69*, 648–655.
11. GHORMLEY, R. K., POLLOCK, G. A., HALL, B. E., and BEIZER, L. H. Multiple myeloma. *Surg., Gynec. & Obst.*, 1942, *74*, 242–244.
12. KINNEY, L. C. Multiple myeloma. *Radiology*, 1940, *35*, 667–674.
13. LEVITT, A., and LEVY, D. S. Multiple myeloma. *Ann. Int. Med.*, 1942, *17*, 863–873.
14. PAUL, L. W., and POHLE, E. A. Solitary myeloma of bone. *Radiology*, 1940, *35*, 651–666.
15. TOTH, B. J., and WINTERMANTEL, J. A. Apparently solitary myeloma with subsequent generalization. *Radiology*, 1943, *41*, 472–477.
16. ULRICH, H. Multiple myeloma. *Arch. Int. Med.*, 1939, *64*, 994–1016.
17. WALLGREN, A. Untersuchungen über die Myelomokrankheit. *Upsala Läkaref. Förh.*, 1920, *25*, 113–263.

Vol. 63, No. 6

OSTEOPETROSIS

REPORT OF A CASE AND REVIEW OF RECENT LITERATURE

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A RATHER rare and interesting abnormality of osseous development was first described by a German roentgenologist, Albers-Schönberg, in 1904. He was able to differentiate his case from those reported by several other authors who had noted osteosclerosis associated with primary blood dyscrasia. He called the disease "marble bones" because of the characteristic dense appearance of the skeletal system. This condition is also known under the names of osteopetrosis (stony bone), Albers-Schönberg's disease, osteosclerosis fragilis generalisata, and congenital osteosclerosis.

Since the original paper, 156 cases have been reported in the world literature. The case reported by us would be the 157th.

Some confusion is present in the literature concerning the criteria necessary to diagnose osteopetrosis. This condition is characterized by increased density of the cortical and medullary portions of the entire osseous system; anemia; and enlargement of the liver, spleen, and lymph nodes. It can be readily seen that differentiation from similar, though unrelated, disease entities is not easy. Pines and Lederer[4] believe that a number of the reported cases are in reality instances of primary disease of the blood with secondary osteosclerosis and myelofibrosis.

The diagnosis of osteopetrosis rests mainly upon the roentgenologist as the primary findings are entirely osseous. However, this disease can be recognized clinically by the secondary changes produced. This is especially true in infants and younger persons, as the severe form of the disease is usually seen in the lower age group and affords early clinical recognition. The more benign form of the disease may produce few secondary changes and often is not recognized unless a fracture or an illness of some type makes a roentgen study necessary.

Roentgenologically, the bones of the entire skeleton are homogeneously opaque. The vertebrae, the pelvis, the skull, proximal end of the femurs, and distal end of tibia and fibula are most severely affected. The trabecular structure of the bones is partially or completely obliterated, and the medullary canal is reduced in size or absent. Usually, the bones are of normal length, but there may be some change in contour. Clubbing of the ends of the long bones, especially of the proximal humerus and distal femur, may be present. Another characteristic feature is the transverse and longitudinal bands of greater and lesser density. Usually seen are the transverse bands, which run through the metaphysis of the long bones, parallel to the epiphyseal line. Occasionally, longitudinal lines are found in the diaphysis parallel to the periosteum. Roentgenologic evidence of rickets is present in some infants.[3] In the skull, suture lines are often wider than normal, the posterior clinoid processes are clubbed, and the sella turcica is shallow. The paranasal sinuses and mastoid cells are often not pneumatized, or only partially so, and the base of the skull is narrowed in an anteroposterior diameter and very dense. Overgrowth of the jaw is frequently present. These changes in the skull are usually quite characteristic of osteopetrosis.

Clinically, several signs produced by this disease are usually present, the most important of which are (*a*) multiple fractures, which usually occur with very slight or even no trauma. These fractures usually heal in a normal time, although several reports of very slow union have been pub-

lished; (*b*) optic atrophy, which is produced by narrowing of the optic foramina. A bony impingement and thickening of the base of the skull accounts for this change; (*c*) anemia, varying from a mild form to a severe aplastic type. It is usually hypochromic. The peripheral blood shows immature red cells, chiefly normoblasts. The platelet count is normal or low. In severe cases of anemia, a tendency to bleed from skin or mucous membranes is found. The leukocyte count is usually low in adults and high in children. Anemia secondary to osteopetrosis is thought to be due to a mechanical interference with the hemopoietic centers in the bone. The marrow that remains is diminished in amount, but active; (*d*) lymphadenopathy, hepatomegalia, and splenomegalia are thought to be due to these structures acting as accessory blood-forming centers.

In addition to these important changes, several others should be mentioned. Children who have the more severe form of the disease show a broad face with a senile expression, a wide, flat nose, thickened lips, prominent frontal bosses, and a wrinkled skin. The patient is underdeveloped. Walking, talking, and dentition are delayed. However, bone growth and epiphyseal appearance are not unusual. Hydrocephalus, deafness, nystagmus, osteomyelitis, and subarachnoid hemorrhages may be seen. The cranial nerve changes are due to narrowing of the various foramina of the base of the skull. Poor dentition and blood supply in the mandible and maxillae may cause marked dental caries with a spreading facial bone infection.

Incidence. Osteopetrosis has been diagnosed in utero and in elderly patients. However, the more typical forms of the disease are usually seen below the age of ten. No characteristic distribution as to race or sex is present.

Etiology. In the total series of cases reported, familial occurrence has been so striking that most authors believe the disease is carried in certain family groups as a recessive mendelian character. A high incidence of consanguinity has also been found. But this does not explain just how the changes are finally produced. Recent authors have found a metabolic condition resembling a chronic hyperparathyroidism in their infant patients.[3] They do not know whether its origin is maternal or fetal. At present, some type of faulty calcium and phosphorus metabolism is believed to be found in osteopetrosis by these authors. Chronic fluorine and phosphorus poisoning produce bony changes similar to osteopetrosis.

Pathology. A recent careful histopathological study of an infant dying of secondary changes of osteopetrosis has been reported by Pines and Lederer.[4] They found marked changes in the epiphyses, metaphyses, diaphyses, and cortex of various bones, and their findings appear to confirm the concept that the pathogenesis of the disease is related to diseased vascular and osseomedullary anlage.

More specifically, they found the epiphyses and metaphyses not prepared for normal bone growth, and a normal, cellular, primary marrow was lacking. An avascular fibrous connective tissue was present instead of the usual marrow at the epiphyses. The different zones of cartilage cell proliferation, maturation, and degeneration were small and poorly developed. The areas of column formation were narrow and irregular. A dense network of chondro-osteoid tissue and minute marrow spaces containing connective tissue marrow was present in the metaphyses. The surface of the cartilage bones and marrow spaces contained large amounts of calcified osteoid tissue.

In the submetaphysis, no lamellar bone is produced because of the absence of osteoclastic and chondroclastic marrow cells, so that the dense chondro-osteoid tissue remains unchanged.

The diaphyses of the long bones also showed changes, particularly in the medullary canals. These structures contained the sclerotic calcified chondro-osteoid substance noted before.

Contrary to most of the literature, Pines and Lederer[4] reported changes in the cortex and periosteum of all bones. The cortex was irregularly widened and consisted mainly of layers of parallel trabeculae of reticular bone. It contained less vascular and hemopoietic tissue than normally found. The periosteum showed numerous areas of one type of fibro-osseous metaplasia.

A generally poor vascularization of the skeleton has been found. It is thought that this is an important factor in the hyperostosis and hypermineralization found in osteopetrosis. However, in areas of healing fractures, vascularity and structure of bone approaches normal.

The primary cause of all these factors is thought to be due to an abnormality of the undifferentiated mesenchymal anlage of the skeleton and bone marrow. When the sclerogenous elements of this anlage are mainly involved, the benign, slow, clinical course occurs, even though the bone structure is greatly altered. Abnormality of the myelogenous portion of the anlage causes malignant and fatal changes, such as is often found in infants.

Zawisch-Ossenitz,[6] in her excellent paper published a few months before the work of Pines and Lederer, believes that the anlage and development are essentially normal up to the beginning of the second period of development of each bone. At this point, some unknown agent damages the anlage. The second period she calls that time when the inner layers of the cortex are resorbed from within in order to widen and shape the secondary marrow cavity. This starts about the fourteenth week of intrauterine life for the femur, and at other times as the various bones begin to differentiate. The malformation produced is responsible for the general retardation of absorption. The threshold of response to stimuli which cause resorption is raised, and resorption is arrested at the beginning of the second period for a long time. This interferes with the normal relations between the bone-forming process: deposition and resorption. As a result, there remains a fetal size and shape of the marrow cavity, a thick cortex composed of all the embryonic strata normally removed and an unusual amount of spongiosa.

According to Zawisch-Ossenitz,[6] as the young patient gets older, some type of bone repair occurs so that adults with osteopetrosis show increasing tendency to normal type of bone. However, resorption is apparently slowed down at all times, and the deposition-resorption cycle remains pathological in some degree.

The explanation of the clubbing seen on roentgenograms of the long bones is stated by Zawisch-Ossenitz to be the result of the hyperplasia and persistence of less differentiated types of bone tissue in the metaphyses. The greater density of bone is due partly to a greater density of structure when the bones are in a state of repair and partly to a higher calcium content. The bands of varying density are caused by periodic remissions or exacerbations of the pathologic deposition of bone by periodic recurrence of widespread resorption. Zawisch-Ossenitz thinks the anemia of osteopetrosis may be due to a relative lack of a substance normally released by bone resorption and which stimulates hemopoiesis.

Although the blood chemical studies of patients with osteopetrosis are usually normal, the bones in this disease show an altered chemical composition. Analysis of bone shows hypermineralization, as indicated by a high ratio of inorganic to organic matter and an increase of the molecular ratio of calcium carbonate to calcium phosphate.[3] These changes increase the brittleness of the bones. Other factors which contribute to the relative weakness of the bones are (*a*) the lack of mature lamellar bone. The chondro-osteoid tissue present does not have the quality, quantity, or arrangement of collagenous fibers and cement substance found in normal bones, and (*b*) the uncontrolled variability in size and shape of bone trabeculae and their

purposeless architectural arrangement.

Prognosis. Previous comments in this paper have indicated a benign type of the disease which has few clinical symptoms, and the changes in the bones are found only incidentally. These patients usually live to normal ages and die of some process not related to osteopetrosis. In the malignant type, death may be early due to intercurrent infections. Osteomyelitis, especially of the mandible and maxilla, is a frequent cause of death.[1] Other causes of death are anemia and hemorrhage. If death does not occur, children with this disease are often marked for life by hydrocephalus, blindness, deafness, multiple fractures, and various physical abnormalities.

Differential diagnosis. Certain other conditions produce increased bone density and some of the clinical signs of osteopetrosis. Many of these diseases can be ruled out without too great difficulty by history, biopsy, roentgenological examination, and laboratory studies. A list of the more common diseases which may be confused with osteopetrosis are syphilis; leukemia; tuberculosis; lead, phosphorus, and fluorine poisoning; hypervitaminosis D or A; Paget's disease; Hodgkin's disease; acromegaly; newborn physiologic osteosclerosis; and myelosclerosis.[5] Several rarer diseases are condensing osteitis of Sicard, eburnating osteitis of Putti, melorheostosis of Léri, ivory vertebrae, and leontiasis ossea.

Treatment. No therapy for the primary lesions is known. Symptomatic treatment is used to relieve secondary manifestations and prolong lives. Anemias are treated by the usual means. Prevention of trauma and prompt treatment of oral or general infections are essential. Careful attention to oral hygiene is necessary. The administration of ergosterol, cod liver oil, calcium, and phosphorus should be avoided, as these might promote further growth of bone.[5] No effective way to alter the mineral content of the bones is known.

Another approach to therapy is suggested by Zawisch-Ossenitz.[6] If the vicious cycle of deposition-resorption abnormality could be broken by stimulating the resorption of bone, she believes improvement could be obtained in those patients who present a chance for survival.

CASE REPORT

The patient is a twenty-one year old, married, colored, female housewife, first admitted to the University Hospital on March 21, 1946, with the chief complaint of repeated broken bones and more recent swelling and pain in the left thigh on motion. She has been followed in the University Hospital Out-patient Department since August, 1933, when, at the age of seven, she fell while skating and broke her left tibia. A long series of fractures followed this apparently original injury. In August, 1936, the left tibia was refractured as the result of a fall. In November, 1938, a fracture of the right femur occurred. A fracture of the right tibia was found in August, 1939, and the left tibia again was broken in November, 1940. All these fractures were treated by routine methods, including immobilization by plaster casts, and apparently healed in the usual time and with good function. In 1938, she had an uneventful recovery from a tonsillectomy, done because of repeated sore throat. In January, 1944, she had a left lower molar extracted because of caries with abscess formation. Following this, she had a soft tissue infection, which spread to both sides of the jaw and produced a low grade fever and cervical lymphadenopathy. Under conservative therapy, the infection subsided. Also about this time, a routine checkup in the medical clinic revealed no important physical abnormalities. The primary cause of this patient's difficulty had not yet been correctly diagnosed. In October, 1944, the patient returned to the clinic complaining of pain in the left thigh, which had persisted since a fall four months previously.

Roentgen examination showed an incompletely united fracture of the left femur. Immobilization was done, but union occurred very slowly, and a year passed before the patient could walk without crutches. At the time of this injury, the patient's history was reviewed, and a more complete examination of the skeleton obtained, On the basis of these films, the final diagnosis was made.

In February, 1946, the patient had pain in the left thigh on weight bearing, and began to use her crutches again. One month before ad-

mission a firm, tender mass in the left thigh with slight shortening of the left leg was noted. Roentgenograms revealed a refracture of the left femur, and the patient was admitted for open procedure on this femur. The remainder of the patient's history is not helpful. She said she has always been short with stubby hands and feet. She has had no major operations or serious illnesses.

No history of familial incidence in this patient's family is found. Three siblings died in infancy of unknown causes. Speculation concerning the causes of these deaths would be useless. The parents are living and well. The patient states that her mother and father are first or second cousins.

A review of the systems shows no important symptoms of osteopetrosis. She had had no significant symptoms of anemia or cranial nerve lesions. However, she has worn glasses since the age of nine. She can see very well without glasses and does not think her eyes are getting worse. She cannot see well for close work, and refraction of eyes in 1940 and 1943 revealed hyperopia with normal discs. The patient also noted occasional buzzing in her ears, usually under an emotional strain. She has been married three years and has no children.

Physical Examination: Blood pressure, 104/50; pulse, 88; respiration, 20. The patient is a short, stocky, colored female in no distress. Skin is clear. No generalized lymphadenopathy is present.

The head is symmetrical. The suture lines are separated, and the fontanelles are open. The frontal bosses are prominent, and the superciliary ridges are flat. The maxillae and malar bones do not present the usual prominence of the maxillary sinuses. A normal sharp angulation of the mandible bilaterally is not present. The ears and eyes are normal. The nose is normal except for a flattening of the bridge. The optic discs and vessels are not unusual. In the mouth, only the teeth, which are rather carious, show any abnormality.

The neck contains several non-tender submaxillary nodes bilaterally.

The chest shows the breasts, heart, and lungs not remarkable.

The abdomen is slightly obese. The liver is palpable 3 cm. below the costal margin. The spleen is not felt.

The extremities show the left leg to be 3 cm. shorter than the right. The left thigh has a tender, firm mass 8 cm. in diameter on the anterolateral aspect. The fingers and toes are stubby, this being mainly due to shortening of the distal phalanges. These are also clubbed. Nails are rough, irregular, and brittle. The longitudinal striations are heavy. Peripheral vessels and deep reflexes are not pathological.

On March 22, 1946, the hemoglobin was 66 per cent (Sahli), and red blood cell count was 3.8 million. The white blood cell count was 6,650. The differential count was 52 per cent polymorphonuclears (all filamentous), 34 per cent lymphocytes, 8 per cent monocytes, 4 per cent eosinophils, and 2 per cent basophils. The corrected sedimentation rate (Wintrobe) was 10 mm. The hematocrit was 33 per cent, and reticulocytes were 0.8 per cent. The red blood cells showed 1 plus anisocytosis, poikilocytosis, and hypochromia. The platelets were slightly reduced. The serum test for syphilis was negative. On June 5, 1946, the hemoglobin was 55 per cent; the white blood cell count was 8,300.

The urine on admission was essentially normal. Sulkowitch urinary calcium excretion was 1 plus. Several other urine examinations were not abnormal. The range of the dilution-concentration urine test was specific gravity 1.024–1.002. The phenolsulfonphthalein test (intravenous) showed 80 per cent excretion in two hours. Stools were not unusual. A satisfactory basal metabolic rate test was minus 6 per cent.

Admission blood chemical studies showed urea nitrogen of 13 mg. and sugar of 79 mg. per 100 cc. Albumin-globulin ratio was 4.6 to 2.05 gm. per 100 cc. Blood cholesterol was 176 mg. per 100 cc. Calcium was 10.2, and phosphorus 4.66 mg. per 100 cc. Acid phosphatase was 0.49, and alkaline phosphatase, 2.11 Bodansky units. These are considered to be within normal limits. On March 27, 1946, blood calcium was 10.0 and phosphorus 3.9 mg. per 100 cc. Alkaline phosphatase was 2.61 Bodansky units. The 17-ketosteroid was 0 per cent. This was repeated on June 21, 1946, and was found to be 0.1 mg. per twenty-four hours.

A pathological report on fragments from the left femur, taken at the time of plating the fracture of this bone in the midshaft, states as follows:

"Section consists of irregular trabeculae of varying grades of calcification and of distorted lacunae. Marrow is composed almost wholly of dense fibrous tissue. Impression: Characteristics of this bone are compatible with osteopetrosis."

Briefly, the hospital course of this admission

showed the patient to have had the fractured left femur openly reduced and plated with a vitallium Lane plate. Chip bone grafts from the iliac crest were placed about the plated area. She was put on a high vitamin diet, but callus formation was poor and union not complete at time of discharge on July 2, 1946. Thyroid extract was used unsuccessfully for a short time. She was sent home in a hip spica.

The roentgen reports which are important diagnostically begin with the report on both hands and the left leg taken on October 30, 1944. At this time, an absence of development of the distal portions of the distal phalanges of both hands was described. The epiphyses for the distal phalanges were present and appeared normal. The report states in part:

"The remainder of the bones of both hands are normal except for a marked increase in density and increase in thickness of the cortices of all bones. The joint spaces are normal" (Fig. 1).

"Roentgen examination of the left tibia, fibula, and femur likewise shows marked increase in the density of all the bones. The cortex of the bones is much more thickened than normal."

The remainder of the report describes partially healed fractures of the left femur and of the tibia. The impression was:

"Congenital absence of the distal portions of the distal phalanges of both hands. Old fractures of left femur and tibia."

On November 14, 1944, another report states:

"Roentgen examination of the skull (Fig. 2 and 3) demonstrates marked increase in the density of all the cranial bones. There is no apparent increase in the thickness, but the diploic portion of the cranial bones is much more narrowed than normally seen. The coronal and sagittal sutures are still separated, although the coronal is only slightly so. The sagittal suture is 3 mm. wide. The lambdoidal suture is much wider than the others, measuring between 8 and 9 mm. in width. There are two rarefied, spongy type areas in the posterior parietal region bilaterally, each being approximately 4.5 cm. in its greatest diameter. This apparently involves the inner table of the parietal bone. The sella turcica is smaller than normal, and the anterior and posterior clinoid processes are fused.

"The angle of the mandible at the junction of the ramus and the condyles is straight. This

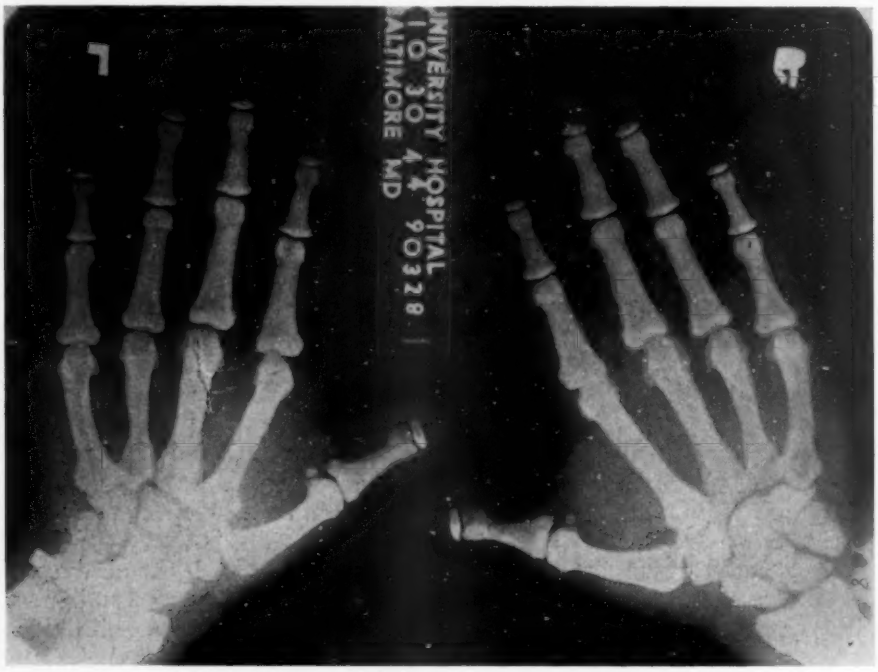

FIG. 1. The distal phalanges show a marked dysplasia. The structure is dense, and the cortex is thickened in all bones.

Fig. 2. The skull shows the widened sutures and unclosed anterior fontanelle. Note the absence of the paranasal sinuses.

Fig. 3. The areas of dysplasia in the parietal bones are demonstrated. Also note the small, enclosed sella turcica, the configuration of the mandible and the narrow, thick skull base.

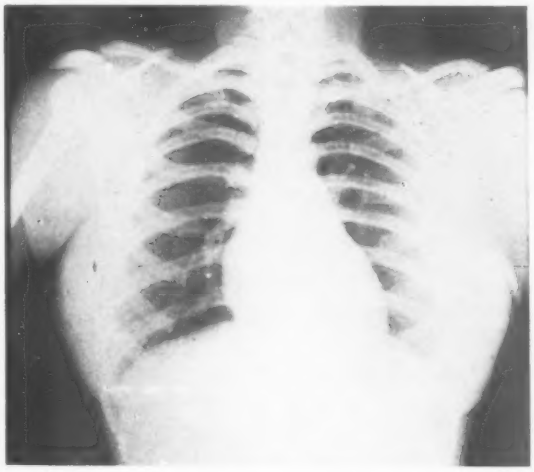

Fig. 4. Thickening of the rib cortex is well seen. Other bones show typical changes. Medullary canals are narrowed.

Fig. 5. Note the generalized increased bone density, the scoliosis and the elongated femoral necks. Bones are homogeneous in appearance. The trabeculae are poorly defined.

bone likewise is much denser than normal.

"Roentgen examination of the chest (Fig. 4) demonstrates the heart and great vessels to be of average size. The lungs and costophrenic angles are clear, and there are no definite pleural changes. All the ribs and both shoulder joints show marked increased density, which was described for the other bones.

"The pelvis and spine show S-shaped scoliosis, involving the lower thoracic and upper

lumbar vertebrae. Similar increase in density is present in all the lumbar spine and pelvis. The hip joints are normal, but the necks of the femora are much longer than is seen for bones of this size." (Fig. 5)

"Impression: Osteopetrosis of the skull, chest, and bony structures of the lumbosacral spine and pelvis."

The paranasal sinuses, which were not described on this report, are not developed or aerated. The mastoid cells are also poorly developed and aerated. The posterior and anterior fontanelles also remain widely separated, and fusion of bone in these areas is poor. Examination of the feet (Fig. 6) is described as follows:

FIG. 6. Changes in the feet are similar to those of the hands. Dysplasia of the distal phalanges is present.

"The feet show a condition similar to that described in the hands. There is marked hypoplasia of the distal phalanx in each toe." An incomplete fracture in one of the toes was described, and the impression was again osteopetrosis.

From this time on, many roentgen examinations were done to follow the fracture of the left femur with plating, and the other various fractures which have been described, such as the fracture of the sacrum and the left forearm at the elbow. None of these reports contribute to the case except to keep a record of the slow healing of the left femoral fracture, even after bone grafts. The final reports in April and May, 1948, show the fracture of the left femur to be in satisfactory position, but some absorption occurring about the bone graft with very little evidence of callus formation.

A second admission occurred on December 9, 1947. She had done well after her previous admission until October 3, 1947, when she fell down a flight of steps and refractured her left femur just below the Lane plate. At the same time, the left radius, and the sacrum were fractured. The forearm and sacral fractures united satisfactorily before this admission, but the femoral fracture was not healed.

Physical and laboratory examinations showed no important change from before. For unavoidable reasons, the patient was discharged in a few days to return later for treatment.

The patient was readmitted on December,

17, 1947, for surgical treatment of the old ununited fracture of the left femur.

The physical examination was not different from previous admissions, and no further abnormalities were noted.

On January 5, 1948, a plate readjustment was done, using the plate put in at the previous operation. An "onlay" heterologous bone graft was also done, using the patient's husband as donor. A bone biopsy taken at this time showed some areas of normal bone, with other regions showing rarefaction or sclerosis. The marrow was fibrotic. The impression was "osteitis fibrosa, consistent with clinical osteopetrosis."

FIG. 7. The ununited left femur is seen before plating. Note the pathological type fracture and inadequate callus formation.

FIG. 8. The left lower leg shows the typical bone changes of osteopetrosis. Old healed mid-tibial fracture is seen.

Following operation, patient had temperature elevation to 102.6° F. On penicillin therapy, this dropped to normal limits. The remainder of the hospital stay was uneventful, and she was discharged on February 12, 1948, in good condition and in a hip spica. While in the hospital, she was on a low calcium diet, but no other specific treatment was given.

On admission, hemoglobin was 11.0 gm. (80 per cent), and white blood cell count 6,200. Urine was essentially normal. Shortly before discharge, hemoglobin was 10.2 gm. (71 per cent); red blood cell count 4.34 million; white blood cell count 7,150. Urine was again negative.

Serological test for syphilis was negative. Blood urea nitrogen and blood sugar were in normal limits. Three days after operation, blood calcium was 9.5 mg., and phosphorus 3.5 mg. per 100 cc. Alkaline phosphatase was 2.5 Bodansky units. Just before discharge, blood calcium and phosphorus were 10.2 and 6.0 mg. per 100 cc. respectively.

Roentgen examination of the left femur showed the old fracture to be reduced in good position and a moderate callus forming about the bone graft of fracture area.

This patient later was seen as an outpatient. The spica was removed, and when last seen (May, 1948), she was walking well and had no complaints.

COMMENT

A case of osteopetrosis is presented. This patient has the characteristic roentgen

findings described in the literature for this disease. The changes in the skull are quite marked. Clinically, the patient can be classified as the benign type, as she has survived to the age of twenty-one and has only a few of the typical secondary changes. She has had multiple fractures, several of which, especially of the left femur, have poor union. It is more usual to find the union occurring in a normal time. She has no demonstrable cranial nerve lesions. Her anemia is not severe, and generalized adenopathy is minimal.

Two unusual features of this case are (1) the spongy type of bone formation in the parietal bones bilaterally, and (2) hypoplasia of terminal phalanges of fingers and toes. In the English literature, we have not found these changes previously described as associated with osteopetrosis. We can offer no adequate explanation for either of these changes in the absence of biopsy studies, particularly of the skull. In this area, the appearance is hypo-ossification rather than hyperossification. It is suggestive of a fibrous dysplasia. Pines and Lederer[4] mention a type of fibro-osseous metaplasia in the periosteum of a bone, which they studied. A congenital abnormality coincident with, but not caused by osteopetrosis, could explain the phalangeal abnormality. Syndactylism and achondrodysplasia are described as sometimes being seen with osteopetrosis.[1] Some similar type of congenital abnormality may also be the explanation of the skull changes.

In a review of the literature, nothing new has been advanced to explain the primary etiology of osteopetrosis since the less recent papers. Pathologically, recent papers agree essentially that some factor is present which affects adversely normal bone-forming processes in the fetus. This occurs very early in development, probably at the so-called second period of ossification. The defect is apparently of the primary mesenchymal anlage. A hormone factor of either fetus or mother, producing abnormal calcium-phosphorus metabolism may also play a primary role in the pathological process.

The end result is poor differentiation of bone, and persistence of fetal type chondro-osteoid tissue in all parts of bone, due to inadequate resorption. This, along with hypermineralization, and architectural changes of trabeculae, produces the increased brittleness of the bones.

No advances in therapy of this disease have been found.

CONCLUSION

(1) A typical case of osteopetrosis of the benign type has been reported.

(2) Two unusual features, not previously seen in the English literature, are present in this case. We cannot adequately explain them. They may be due to some other type of congenital abnormality associated with osteopetrosis.

(3) A review of the recent literature has shown a careful study of the pathology and osteogenesis of the disease by several authors. They have answered adequately many former problems and confirmed some of the earlier work, but many questions still remain.

(4) There is still no adequate therapy for this disease.

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REFERENCES

1. HIGINBOTHAM, N. L., and ALEXANDER, S. F. Osteopetrosis; four cases in one family. *Am. J. Surg.*, 1941, *53*, 444–454.
2. LINDAHL, W. W., MOKROHISKY, S. M., and RITOTA, M. C. Albers-Schönberg disease affecting soldier. *Texas State J. Med.*, 1946, *42*, 37–39.
3. PINCUS, J. B., GITTLEMAN, I. F., and KRAMER, B. Juvenile osteopetrosis; metabolic studies in 2 cases and further observations on composition of bones in this disease. *Am. J. Dis. Child.*, 1947, *73*, 458–472.
4. PINES, B., and LEDERER, M. Osteopetrosis; Albers-Schönberg disease (marble bones). *Am. J. Path.*, 1947, *23*, 755–781.
5. WINTER, G. R. Albers-Schönberg disease. *Am. J. Orth.* (Oral Surg. Sect.), 1945, *31*, 637–649.
6. ZAWISCH-OSSENITZ, CARLA. Marble bone disease; study of osteogenesis. *Arch. Path.*, 1947, *43*, 55–75.

Vol. 63, No. 6

TERATOMATOUS TUMORS OF THE SPINAL CANAL

REPORT OF TWO CASES*

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TERATOMATOUS tumors are developmental tumors containing one or more germ layer elements in varying degrees of organization and differentiation.[1,8,13,15] Such tumors of the spinal canal are uncommon. Rasmussen, Kernohan and Adson[18] in their review of 557 tumors of the spinal canal reported only 3. There have been approximately 80 developmental tumors recorded[2,6,9,11,12,14,16,19] to date. Since they are uncommon, we are reporting a subdural epidermoid and a subdural mixed tumor of the spinal canal primarily to emphasize the roentgenologic features.

CASE REPORTS

CASE 1. A white woman, aged forty-five, entered the Cleveland Clinic on May 9, 1945, with the chief complaints of pain, numbness, and weakness in the legs and back. She dated the onset of pain, her first symptom, to a fall in childhood. The pain was so severe in the low back and thighs that she was in bed for approximately one year. Following this she experienced remissions and exacerbations of pain over the years, and in 1922 was again forced to go to bed for several weeks. She again improved. In 1937 she first noticed a weakness of her right leg and had difficulty controlling her foot. About five years later her left leg became weak. In January, 1945, she was unable to walk for a period of about an hour. The legs were "limp." Since this episode she had noticed numbness of both legs and the distal trunk. She claimed that this feeling caused urinary frequency. In the past two weeks, the pain had been much worse and awakened her at night. It was aggravated by coughing, sneezing, straining, sitting, standing and walking.

Physical examination revealed tenderness over the lumbosacral region. There was limitation of flexion, extension, and lateral bending of the lumbar spine. There was weakness of both legs and feet which was more severe on the right. The Achilles reflex was absent bilaterally. There was partial anesthesia below the second lumbar vertebra and complete anesthesia over the lower innervation of the fifth lumbar and first, fourth, and fifth sacral vertebrae.

A lumbar spinal puncture was done and 5 cc. of fluid was removed. The initial pressure was

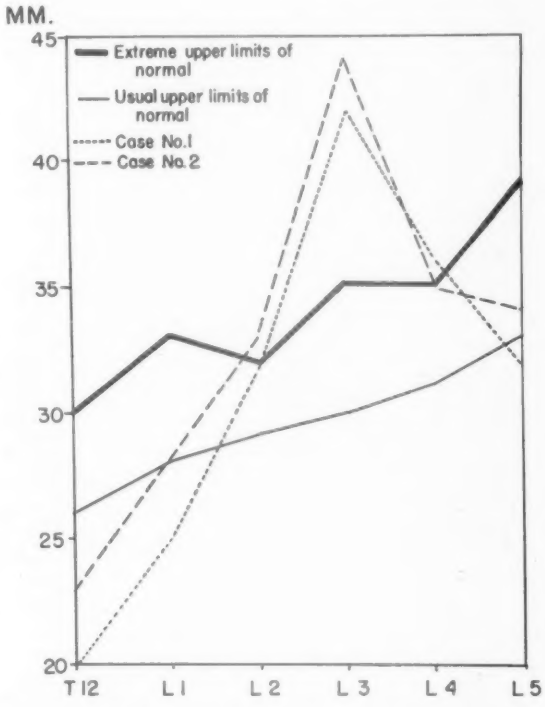

FIG. 1.

110 mm. of water, the Queckenstedt sign was negative; and total spinal fluid protein was 23 mg. per cent. The Wassermann and Kahn tests on the spinal fluid were negative. No cells were present.

Routine laboratory examinations were made. The urine revealed nothing abnormal. The blood showed 13 gm. hemoglobin. The white

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blood cell count was 5,100. The blood Wassermann and Kahn tests were negative.

Roentgenograms of the lumbar spine revealed a fusiform enlargement of the canal with an interpedicular distance (Fig. 1) of 42 mm. at the third lumbar vertebra. There was definite erosion of the pedicles at this level (Fig. 2*A*). On the lateral projection there was considerable erosion of the posterior aspect of the body of the third lumbar vertebra with some early erosion of the second lumbar vertebra (Fig. 2*B*). A spina bifida occulta was present at the first sacral vertebra.

A diagnosis of cord tumor at the level of the third lumbar vertebra was made.

The patient was admitted to the Cleveland Clinic Hospital on May 31, 1945, for surgery. At this time she was beginning to develop bowel and urinary incontinence. On June 1, a lumbar laminectomy was done under pentothal anesthesia. Beneath the arachnoid, a cystic tumor was found extending from the first to the fourth lumbar vertebra. It was attached at its upper end to the posterior surface of the conus medullaris. Leaving its lower end was a structure resembling a thickened filum terminale. The roots of the cauda equina were adherent to the tumor and were dissected free from its anterior surface. Since the small portion attached to the conus was so adherent that it could not be removed without serious cord damage, it was not disturbed.

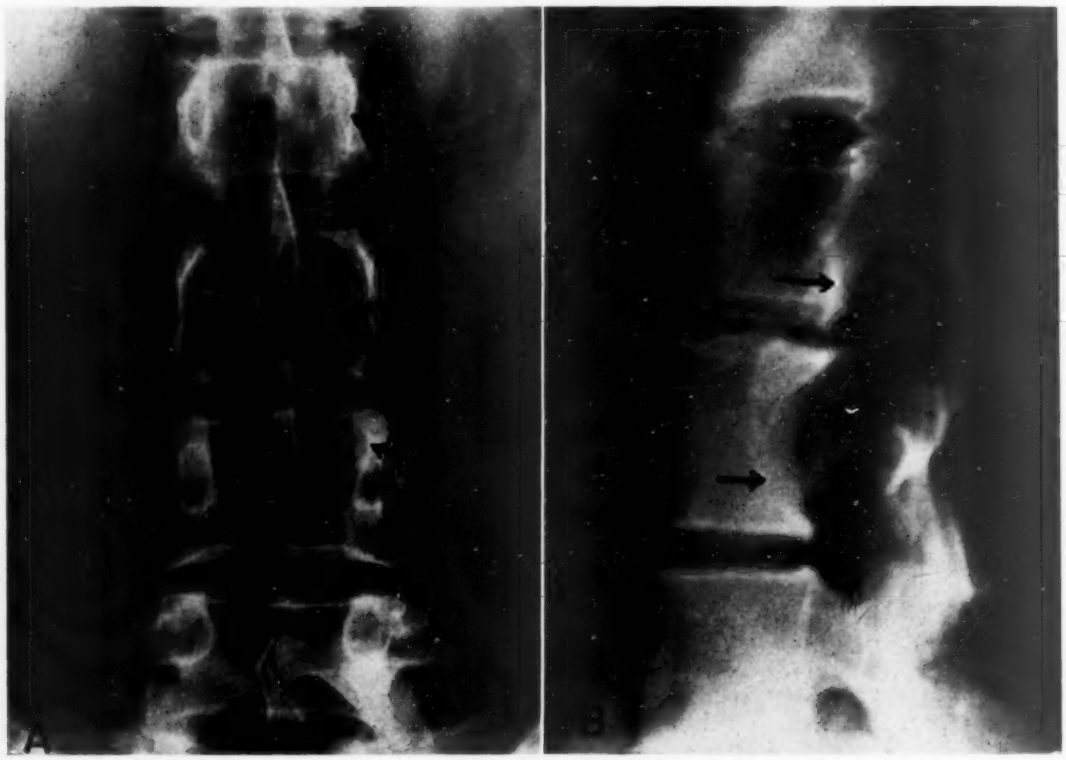

FIG. 2. Case 1. (*A*) Epidermoid cyst. (*a*) Pressure erosion of both pedicles of the third lumbar vertebra; (*b*) minimal erosion of pedicles of the first and fourth lumbar vertebrae (erosion of laminae of the third lumbar vertebra evident on original anteroposterior roentgenogram). (*B*) Erosion of posterior surfaces of the bodies of the second and third lumbar vertebrae.

Gross examination of the specimen revealed a white, thin walled cystic tumor 6.5 by 4.5 by 3 cm. containing yellow-white cheese-like material. The wall itself was only 1 mm. in thickness. Microscopically (Fig. 3), the cyst was lined with stratified squamous epithelium of about six layers of normal cells. The basement membrane was intact. The contents of the cyst contained anuclear keratinized squamous cells. The pathologic diagnosis was epidermoid cyst.

There were no postoperative complications.

On discharge from the hospital on June 23, the patient showed good muscle power with moderate hyperesthesia of the lower extremities. Bowel control was good, but bladder control was only fair.

On November 27, 1945, the patient wrote that she felt better than she had in many years. She was able to walk with a support. The hyperesthesia of the legs was still present but both bowel and bladder control had improved. On April 8, 1947, she wrote that her condition remained about the same.

Fig. 3. Case 1. Photomicrograph of wall of epidermoid cyst (×70).

Case II. A male, white, aged forty, entered the Cleveland Clinic on January 8, 1948, with the chief compiaint of being unable to urinate. He first experienced this difficulty following a lumbosacral "strain" in 1943. He was again troubled in September, 1946, while on a trip and was hospitalized for two days. No genitourinary abnormality was detected at this time. In April, 1947, and again in September, 1947, he had to be catheterized. Since then he has been catheterized three times. He had also been troubled with intermittent low back pain and left "sciatica" since his "strain" in 1943.

Physical examination revealed nothing abnormal except for partial anesthesia over the left buttock and left lower leg and foot.

A lumbar spinal puncture was done and 10 cc. of xanthochromic fluid was removed. The initial pressure was 120 mm. of water. The

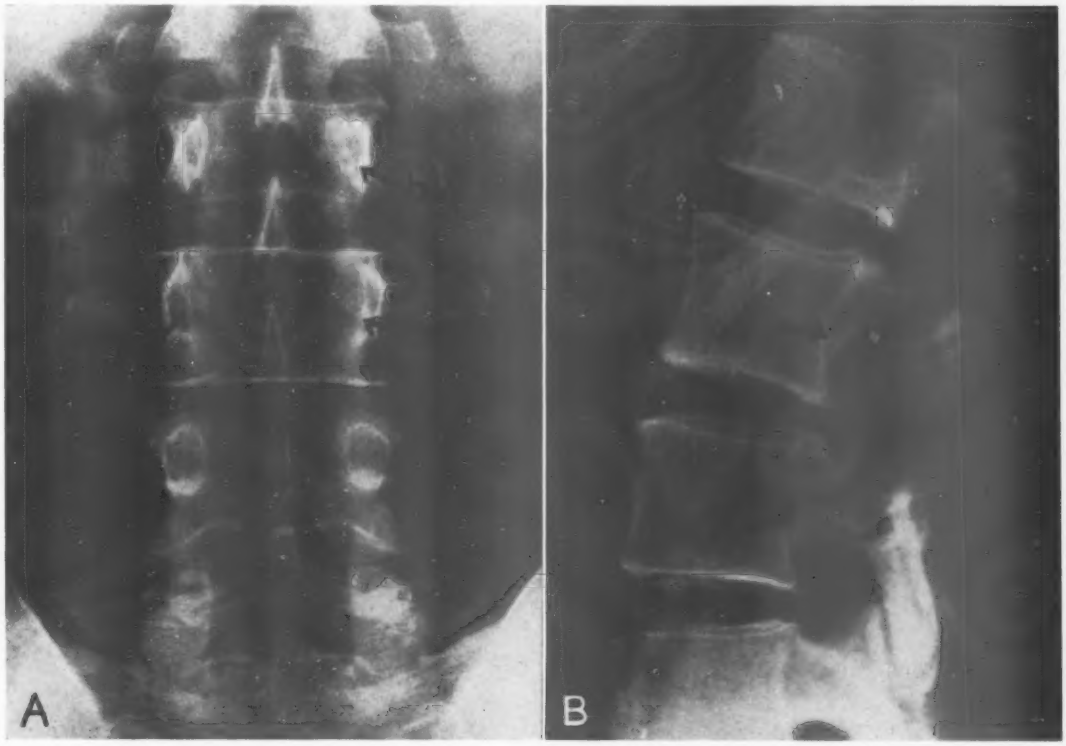

Fig. 4. Case II. (*A*) Mixed tumor. (*a*) Erosion of medial aspects of both pedicles of the third lumbar vertebra; (*b*) minimal erosion of medial aspect of both pedicles of the second lumbar vertebra. (*B*) Lateral projection shows erosion of the posterior aspect of the third lumbar vertebra with some early erosion of the second lumbar.

Queckenstedt sign demonstrated a partial block, and the spinal fluid protein was 850 mg. per cent. The cell count was 15 lymphocytes. The Kahn test on the spinal fluid was negative.

The urine revealed 5 to 15 white blood cells per high power field. The blood showed 13.5 gm. hemoglobin. The white blood cell count was 8,000. Wassermann and Kahn tests on the blood were negative.

FIG. 5. Case 11. Photomicrograph of mixed tumor (×70).

Roentgenograms of the lumbar spine showed a fusiform enlargement of the canal with an interpedicular distance of 44 mm. at the third lumbar vertebra (Fig. 1). There was considerable erosion of the pedicles at this level (Fig. 4*A*). On the lateral projection there was erosion of the posterior aspect of the body of the third lumbar vertebra with some early erosion of the second lumbar vertebra (Fig. 4*B*). A spina bifida occulta was present at the first sacral vertebra.

A diagnosis of cord tumor at the level of the second and third lumbar vertebrae was made.

The patient was admitted to the Cleveland Clinic Hospital on January 14, 1948, for surgery. On January 15 a cystoscopic examination and retrograde pyelogram were normal. On January 16, under pentothal anesthesia, a lumbar laminectomy was done. Beneath the arachnoid there was a large yellowish tumor which blended into the conus medullaris and extended well down into the lumbar region. The tumor was so adherent on its anterior surface that it could not be removed without considerable nerve damage and a subtotal resection was done.

Gross examination of the specimen revealed a dumbbell shaped mass, the upper portion of which was approximately the size of an egg and the lower portion somewhat smaller. In one area there was a brown, hard, partially calcified mass flecked with cholesterin crystals; a second area consisted of a cystic collection of xanthochromic fluid; and a third area in the inferior portion of the tumor consisted of a soft, homogeneous, cheesy material. Microscopically (Fig. 5), there was a mass of macrophages, cholesterol clefts, brown pigment, and fibroblasts walled by fibrous tissue. Adjoining this (Fig. 6) was a mass of fat tissue, fibrous tissue, nerves, glial tissue, and smooth muscle. Stratified epithelium was present at the edge of this area. The pathologic diagnosis was a mixed tumor, a considerable portion of which was "so-called" cholesteatoma.

Postoperatively, the patient developed a urinary infection. On January 26 a suprapubic puncture was done. The patient responded well and was discharged on January 31 in good condition. He returned for examination on April 1, 1948. He stated that he felt exceedingly well and was able to pass his urine normally. There was no muscle weakness and no pain.

COMMENT

Extremely slow growth is one of the most characteristic features of teratomatous tumors. For this reason, it is not uncommon for patients to have mild, gradually progressing symptoms for ten years, and occasionally for as long as forty years, before diagnosis is established.[10,17,20]

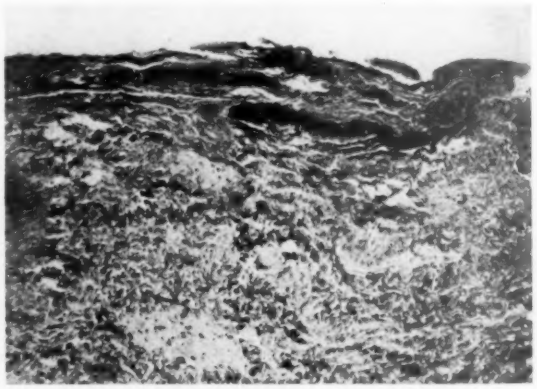

FIG. 6. Case 11. Photomicrograph of mixed tumor (×70).

Camp[4] and Camp, Adson and Shugrue,[3] in reviewing roentgenograms of a large

number of tumors in the spinal canal have estimated that 20 per cent show bone changes on the plain films. Unfortunately, we have been unable to determine the exact number of teratomatous tumors which demonstrate bone change due to incomplete reports in the literature. However, from the reports available we estimate that over 50 per cent exhibit some degree of bone change. These changes are due entirely to pressure. There is frequently a fusiform enlargement of the canal with a great increase in the interpedicular distance. The pedicles may be decalcified, flattened, concave, or eroded.

Elsberg and Dyke[7] have made a study of 300 normal spines, observing the interpedicular distances and appearance of the pedicles. They considered that a decrease in the interpedicular distance was not significant, but an increase of 2 to 4 mm. was abnormal. They believed that flattening of the pedicles was significant only when associated with an increased interpedicular distance. French and Peyton[9] emphasize the correlation between the interpedicular distance and the age of the patient in determining a true increase.

Camp[5] has been able to make a diagnosis of spinal canal tumor in all of a series of 23 cases in which only half showed an increased interpedicular distance. His diagnosis depended largely on the detection of erosion of the laminae. This is frequently difficult to detect in the early stages.

Erosion of the posterior surface of the vertebrae presumably occurs late.

With the use of myelography the presence and the level of a cord tumor can be established with at least 90 per cent accuracy. However, in the teratomatous group it is frequently not necessary to resort to myelography because the diagnosis of cord tumor can be made from plain roentgenograms.

SUMMARY

In two patients with teratomatous tumors, roentgenograms of the spine showed fusiform enlargement of the spinal canal, an increased interpedicular distance, erosion of the laminae, and erosion of the posterior surfaces of several vertebrae.

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REFERENCES

1. Boyd, W. A Textbook of Pathology: An Introduction to Medicine. Fourth edition. Lea & Febiger, Philadelphia, 1943.
2. Boldrey, E. B., and Elvidge, A. R. Dermoid cysts of vertebral canal. *Ann. Surg.*, 1939, *110*, 273–284.
3. Camp, J. D., Adson, A. W., and Shugrue, J. J. Roentgenographic findings associated with tumors of spinal column, spinal cord, and associated tissues. *Am. J. Cancer*, 1933, *17*, 348–372.
4. Camp, J. D. Significance of osseous changes in roentgenographic diagnosis of tumors of spinal cord and associated soft tissues. *Radiology*, 1934, *22*, 295–303.
5. Camp, J. D. Roentgenologic contributions to localization of tumors affecting spinal cord. *Wisconsin M. J.*, 1937, *36*, 621–625.
6. Craig, R. L. Case of epidermoid tumor of spinal cord; review of literature of spinal epidermoids and dermoids. *Surgery*, 1943, *13*, 354–367.
7. Elsberg, C. A., and Dyke, C. G. Diagnosis and localization of tumors of spinal cord by means of measurements made on x-ray films of vertebrae, and correlation of clinical and x-ray findings. *Bull. Neurol. Inst. New York*, 1934, *3*, 359–394.
8. Ewing, J. Neoplastic Diseases: A Treatise on Tumors. Fourth edition. W. B. Saunders Company, Philadelphia, 1940.
9. French, L. A., and Peyton, W. T. Mixed tumors of spinal canal. *Arch. Neurol. & Psychiat.*, 1942, *47*, 737–751.
10. Gross, S. W. Concerning intraspinal dermoids and epidermoids, with report of case. *J. Nerv. & Ment. Dis.*, 1934, *80*, 274–284.
11. Hosoi, K. Intradural teratoid tumors of spinal cord. *Arch. Path.*, 1931, *11*, 875–883.
12. Ingraham, F. D., and Bailey, O. T. Cystic teratomas and teratoid tumors of central nervous system in infancy and childhood. *J. Neurosurg.*, 1946, *3*, 511–532.
13. Karsner, H. T. Human Pathology. Sixth edition. J. B. Lippincott Company, Philadelphia, 1942.
14. List, C. F. Intraspinal epidermoids, dermoids, and dermal sinuses. *Surg., Gynec. & Obst.*, 1941, *73*, 525–538.
15. MacCallum, W. G. A Textbook of Pathology. Seventh edition. W. B. Saunders Company, Philadelphia, 1940.

16. Masten, M. G. Teratoma of spinal cord. *Arch. Path.*, 1940, *30*, 755–761.
17. Naffziger, H. C., and Jones, O. W., Jr. Dermoid tumors of spinal cord. *Arch. Neurol. & Psychiat.*, 1935, *33*, 941–958.
18. Rasmussen, T. B., Kernohan, J. W., and Adson, A. W. Pathologic classification, with surgical consideration of intraspinal tumors, *Ann. Surg.*, 1940, *111*, 513–530.
19. Sjövall, H. Dermoide des Rückenmarkskanas. nebst Mitteilung eines Falles von infizierter Dermoidcyste im Spinalkanal als Ursache einer tödlich verlaufenen Staphylococcus-albus-Meningitis. *Acta orthop. Scandinav.*, 1941, *12*, 1–32.
20. Verbiest, H. Die Epidermoide des Rückenmarkes, Analyse eines Falles, zugleich Beitrag zur Frage der Entstehung der aseptischen Meningitis nach Epidermoidoperationen. *Zentralbl. f. Neurochir.*, 1939, *4*, 129–141.

Vol. 63, No. 6

CANCER OF THE THYROID: TEN TO TWENTY YEAR FOLLOW-UP*

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CANCER of the thyroid, a comparatively rare lesion, represents approximately 1 per cent of all cancers, yet the complexities of malignant tumors of the gland are so numerous that accurate description and factual data have thus far eluded the workers in this field.

The present paper deals with our findings in 198 cases of cancer of the thyroid in which diagnosis was made prior to 1936 and the patients' course was followed. The history and histopathology of each case have been reviewed and all cases were reclassified into the recent classification of Warren and Meissner.**

CLASSIFICATION OF THYROID CANCER

Group I: Adenomas with invasion
  a. Alveolar (fetal) adenoma
  b. Papillary adenocystoma
Group II: Adenocarcinomas
  a. Papillary type
  b. Alveolar type
Group III: Carcinoma simplex
  a. Small cell type
  b. Giant cell type
Miscellaneous
  a. Hürthle cell
  b. Fibrosarcoma
  c. Lymphoma
  d. Epidermoid
  e. Unclassified

This classification as presented deals with histopathologic changes only but is a satisfactory clinical classification for carcinoma, with the exception of the alveolar adenomas with invasion. This tumor, while showing invasion histopathologically, is apparently curable by simple surgical excision and none of the patients with this tumor in our series has shown the usual clinical evidences of cancer.

A review of the histories of these patients indicates that thyroid cancers arise in pre-existing tumors (Table I).

Cancer may occur at any age, yet the more rapidly growing tumors have a predilection for persons past fifty years of age (Table II).

The clinical evaluation of an individual case does not exclude carcinoma. The clinical findings of early cancer are similar to those of single adenomas and thyroiditis, so strikingly similar that biopsy and historical evaluation are necessary for differentiation.

In determining the prognosis and in the treatment of the case, it is always of interest to know the most likely location for metastatic involvement. In Table III the most frequent locations for metastases are

TABLE I

KNOWN PRESENCE OF THYROID TUMOR PRIOR TO DIAGNOSIS

Histopathologic Type	Average Existence of Tumor before Diagnosis
	years
Group I	
Fetal adenoma with invasion	10.8
Papillary adenocystoma	4.5
Group II	
Papillary adenocarcinoma	4.1
Alveolar adenocarcinoma	8.2
Group III	
Small cell carcinoma	5.1
Giant cell carcinoma	15.3

** Meissner, W. A., and Lahey, F. H. Cancer of the thyroid in a thyroid clinic. *J. Clin. Endocrinol.*, 1948, *8*, 749–761.

* Presented at the Thirty-first Annual Meeting, American Radium Society, Atlantic City, N. J., June 5–7, 1949.

TABLE II

THYROID CANCER—AGE AND SEX DISTRIBUTION*

	Cases			Age (years)	
	Females	Males	Total	Average	Range
Group I					
Fetal adenoma with invasion	43	6	49	45.2	20–72
Papillary adenocystoma	41	7	48	46.2	9–70
Group II					
Papillary adenocarcinoma	33	5	38	44.8	13–80
Alveolar adenocarcinoma	19	5	24	44.1	9–70
Group III					
Small cell carcinoma	26	4	30	46.5	9–72
Giant cell carcinoma	8	1	9	59.4	36–70
	170	28	198		

* 80.3 per cent of cases were in Groups I and II.

indicated, although in our experience cancer of the thyroid may metastasize to any part of the body.

In this series, single thyroid nodules were malignant in 10 per cent of the patients coming to operation, a finding which we believe is high enough to warrant removal of all single tumors.

Sixteen patients with cancer in this series had an associated hyperthyroidism, a finding which is likely to have historical significance because all of these tumors were diagnosed prior to the days of radioactive iodine (Table IV). The recent finding of several instances of cancer in patients who had had radioactive iodine or radiation therapy for hyperthyroidism has led some investigators to fear the use of these substances.

Each histopathologic type of thyroid tumor must be considered separately because each acts in a different way and from the standpoint of prognosis and treatment, it is essential to know the type of tumor with which we are dealing.

The alveolar adenomas with invasion, of which there were 49 cases (Fig. 1), were removed surgically and most of the patients were given additional postoperative roentgen therapy. Approximately 6,000 roentgens, measured in air, was given through three portals. There was no evidence of recurrence of this type of tumor in any of the cases that we were able to follow. We

TABLE III

DISTRIBUTION OF KNOWN METASTASES

	Neck	Lungs	Mediastinum	Bone	Soft Tissues	Viscera
Papillary adenocystoma	7	2		1		1
Papillary adenocarcinoma	2	2	1			1
Aveolar adenocarcinoma	4	3	1			1
Small cell carcinoma	6	5		2	2	
Giant cell carcinoma	2	2	2	1		
Total	21	14	4	4	2	3

have recently seen one patient with this type of tumor which was so diagnosed in 1919; the patient was followed in various institutions for thirty years before a small cell type of carcinoma developed. On section, no tumor suggesting an alveolar adenoma with invasion was seen. We therefore believe that while these tumors may be classified as histopathologically malignant, they should not be included as clinical cancer cases.

The papillary adenocystoma with invasion (Fig. 2), of which there were 48 case would probably be better classified clinically as papillary adenocarcinoma as the results following treatment have been similar in both types and their tendency to recur has been almost identical. Here, again, we believe operation should be performed and in all cases in which there is glandular enlargement in addition to the thyroid tumor, radical neck dissection should be carried out. In cases in which there has been invasion of the trachea and muscles, in addition to surgical removal

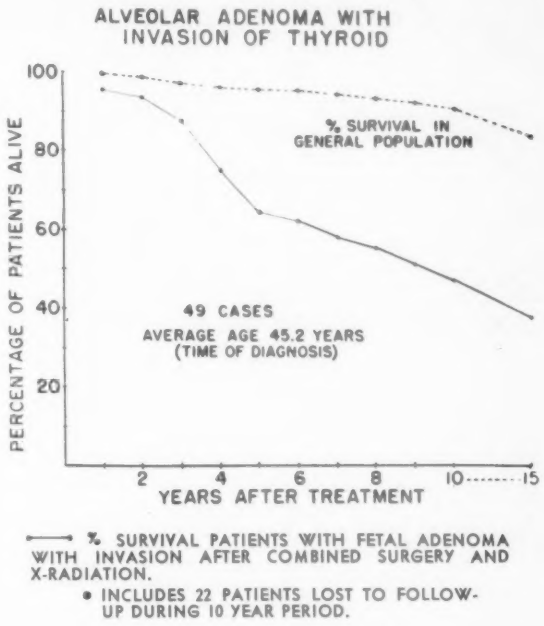

Fig. 1.

Table IV

HYPERTHYROIDISM WITH THYROID CANCER

Type of Tumor	Total Cases	Number and Years Survived		
		Deaths from Thyroid Cancer	Deaths from Other Causes	Alive and Well Last Follow-up
Group I				
Fetal adenoma with invasion	5	0	3 (9 yr.) (18 yr.) (20 yr.)	2 (6 yr.) (20 yr.)
Papillary adenocystoma	7	1 (6 yr.)	2 (3 yr.) (5 yr.)	4 (2 yr.) (8 yr.) (11 yr.) (12 yr.)
Group II				
Papillary adenocarcinoma	2	0	0	2 (6 yr.) (12 yr.)
Alveolar adenocarcinoma	1	0	0	1 (4 yr.)
Group III				
Small cell carcinoma	1	1 (2 yr.)	0	0
	16			

of as much tumor as possible, roentgen treatment, using 6,000 roentgens, air dose,

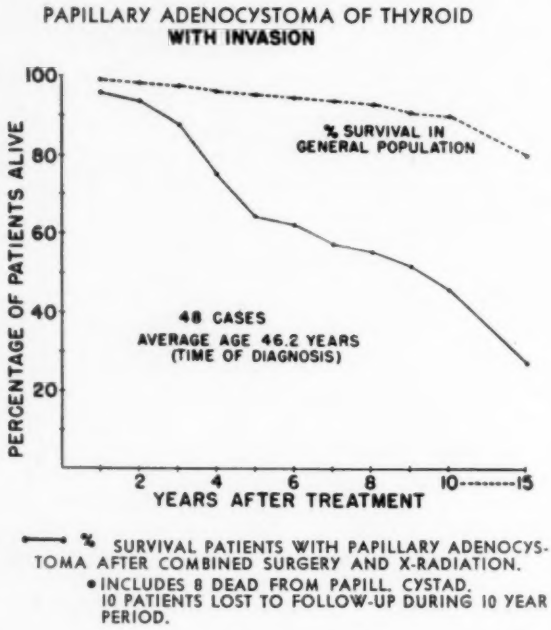
PAPILLARY ADENOCYSTOMA OF THYROID WITH INVASION
PERCENTAGE OF PATIENTS ALIVE
100
80
60
40
20
% SURVIVAL IN GENERAL POPULATION
48 CASES
AVERAGE AGE 46.2 YEARS (TIME OF DIAGNOSIS)
2 4 6 8 10-------15
YEARS AFTER TREATMENT
% SURVIVAL PATIENTS WITH PAPILLARY ADENOCYSTOMA AFTER COMBINED SURGERY AND X-RADIATION.
• INCLUDES 8 DEAD FROM PAPILL. CYSTAD. 10 PATIENTS LOST TO FOLLOW-UP DURING 10 YEAR PERIOD.

FIG. 2.

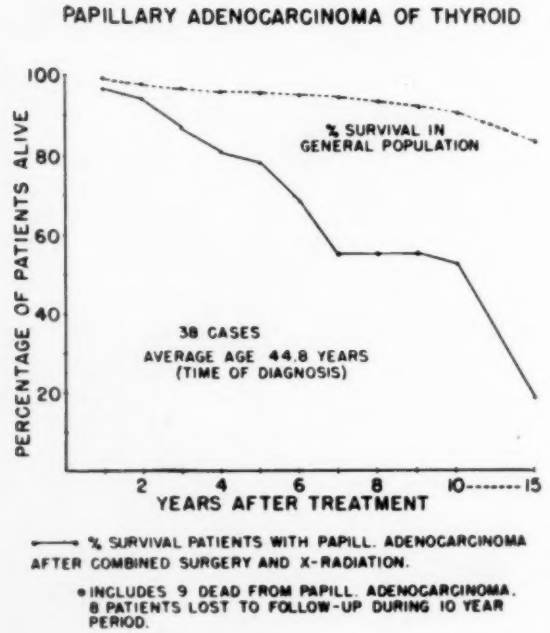
PAPILLARY ADENOCARCINOMA OF THYROID
PERCENTAGE OF PATIENTS ALIVE
100
80
60
40
20
% SURVIVAL IN GENERAL POPULATION
38 CASES
AVERAGE AGE 44.8 YEARS (TIME OF DIAGNOSIS)
2 4 6 8 10-------15
YEARS AFTER TREATMENT
% SURVIVAL PATIENTS WITH PAPILL. ADENOCARCINOMA AFTER COMBINED SURGERY AND X-RADIATION.
• INCLUDES 9 DEAD FROM PAPILL. ADENOCARCINOMA. 8 PATIENTS LOST TO FOLLOW-UP DURING 10 YEAR PERIOD.

FIG. 3.

has prevented recurrence of the lesion. It has been further shown in metastases from this type of lesion that progression of the disease may be inhibited for many years by roentgen irradiation even though the tumor does not entirely disappear (Fig. 1).

Of the Group II carcinomas, the papillary adenocarcinomas of the thyroid (Fig. 3) should be treated in the same way as the papillary adenocystomas. There were 38 patients with this type of tumor and the results of treatment were the same as those following treatment of the papillary adenocystomas.

The tumors thus far described are those which are most likely to respond to radioactive iodine. It would probably be inadvisable to treat patients with alveolar adenomas with invasion following surgical

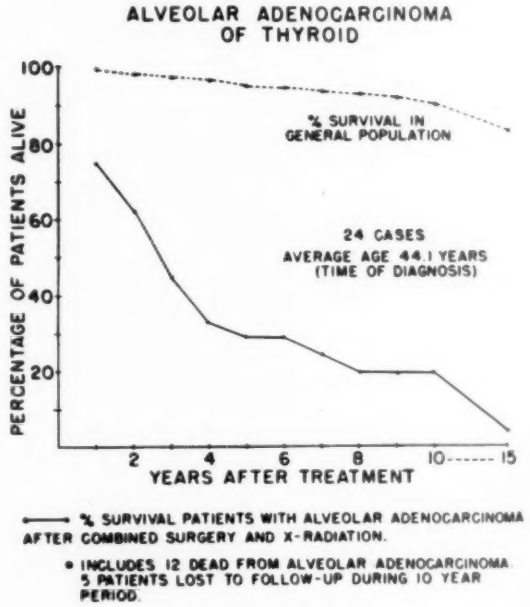
ALVEOLAR ADENOCARCINOMA OF THYROID
PERCENTAGE OF PATIENTS ALIVE
100
80
60
40
20
% SURVIVAL IN GENERAL POPULATION
24 CASES
AVERAGE AGE 44.1 YEARS (TIME OF DIAGNOSIS)
2 4 6 8 10------ 15
YEARS AFTER TREATMENT
% SURVIVAL PATIENTS WITH ALVEOLAR ADENOCARCINOMA AFTER COMBINED SURGERY AND X-RADIATION.
• INCLUDES 12 DEAD FROM ALVEOLAR ADENOCARCINOMA. 5 PATIENTS LOST TO FOLLOW-UP DURING 10 YEAR PERIOD.

FIG. 4.

removal since these tumors are readily curable by simple surgical excision. The results of treatment of the other two tumors indicate that if radioactive iodine is to be successful it would be necessary to use it in only a small percentage of cases, those beyond the scope of surgery and roentgen irradiation. The value of the tracer dose of radioactive iodine cannot be omitted, especially if there are any clinical signs of secondary involvement.

The alveolar adenocarcinoma (Fig. 4)

has been, indeed, a difficult type of lesion to control. In a total of 24 cases the five year survival rate was 29.1 per cent and 3 of these patients who survived required radium in addition to roentgen therapy. Although all these tumors were histopathologically alveolar adenocarcinomas, their response to irradiation was not the same in all cases, perhaps due to a difference in the host.

The alveolar tumor, if it accepts radioactive iodine, may be curable, but there are probably enough anaplastic cells in this type of tumor which will not accept radioactive iodine to make it advisable to use roentgen irradiation, and in some cases, radium, in addition to radioiodine therapy. Especially in the localized, fixed lesions, radium implantation may be of value. Figure 5 illustrates graphically how 2 of the 3 surviving patients were treated, and the third case was similar in appearance to the spherical lesion. These radium charts indicate that a total dose of approximately 6,000 gamma roentgens was applied to the periphery of the tumor, and the largest dose as measured at the point likely to get the greatest dosage was about 11,000 gamma roentgens, which is still within normal tissue tolerance but at the upper limits.

Group III carcinomas of the thyroid represent the small cell and the giant cell types. There were 30 cases with the small cell variety. These tumors are rapidly growing. The incidence of 20 per cent five year survival is indicative of the rapidity of their growth (Fig. 6). These lesions, however, have all proved radiosensitive and if the diagnosis can be made early and treatment instituted, the improvement in results should be noticeable within a short period of time.

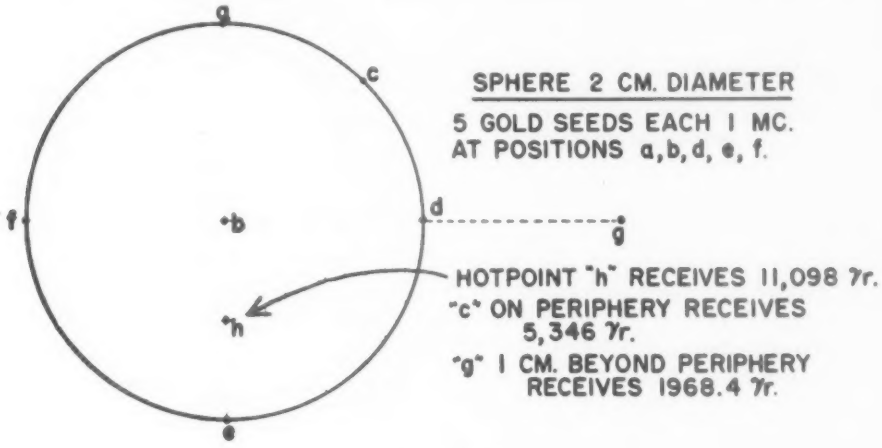

Fig. 5.

Table 1 shows that tumors—at least a

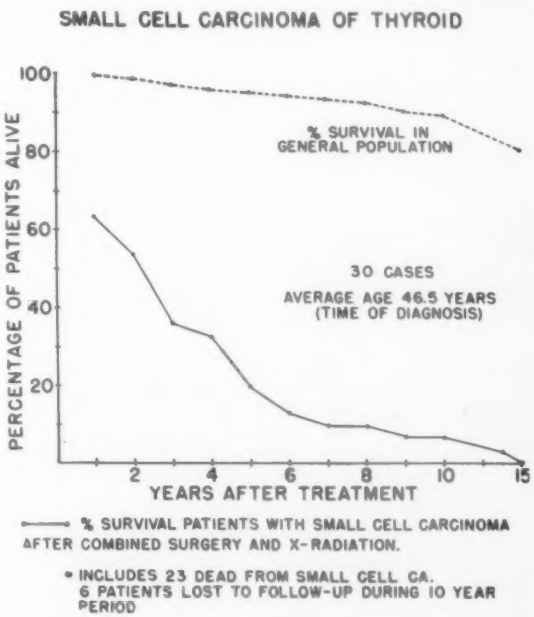

Fig. 6.

thyroid adenoma—are present five years or more prior to the known malignant degeneration. Thus an early diagnosis is possible and imperative if better survival rates are to result.

In the giant cell carcinomas of the thyroid the five year survival rate was 22.2 per cent, but only 2 of 9 patients lived for five years (Fig. 7).

In our experience, giant cell tumors have not been radiosensitive to any amount of roentgen treatment which the normal tissues will tolerate. If a recurrence follows surgery, then we consider the case hopeless.

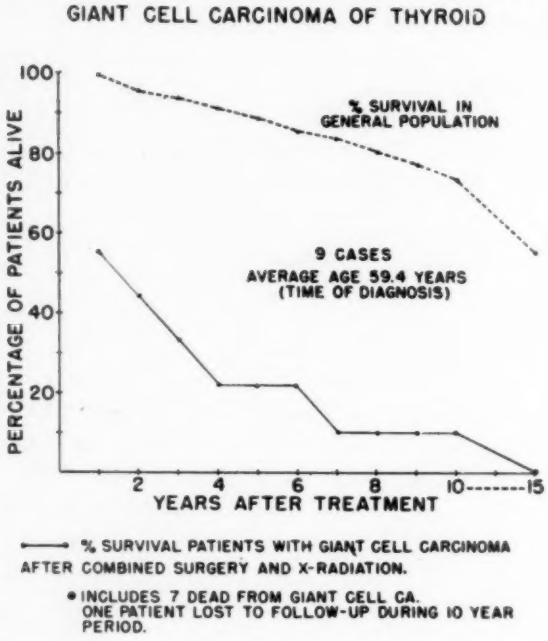

FIG. 7.

TREATMENT OF CARCINOMA OF THE THYROID

The treatment of carcinoma of the thy-

TABLE V

POSTOPERATIVE ROENTGEN TREATMENT FOR CANCER OF THE THYROID: TREATMENT DIRECTED TO ENTIRE TUMOR BED—THROUGH THREE PORTALS, ONE ON EACH SIDE AND ONE IN MIDLINE OF NECK

Total dose—2,000 r per portal Total—6,000 r, measured in air	in 21 days
Factors:	
kv.	200
ma.	20
distance	50 cm.
filter	1 mm. copper and 1 mm. aluminum
portal	75–100 sq. cm.
dose daily to each portal	100 r

TABLE VI

THYROID CANCER—SURVIVAL AFTER TREATMENT: TOTAL 198 PATIENTS

	5 Years		10 Years		15 Years		20 Years	
	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent
Group I								
Fetal adenoma with invasion (total 49 patients)	38	77.5	19	38.7	7	14.2	5	10.2
Papillary adenocystoma (total 48 patients)	31	64.5	23	47.9	13	27.0	2	4.1
Group II								
Papillary adenocarcinoma (total 38 patients)	30	78.9	20	52.6	7	18.4	4	10.5
Alveolar adenocarcinoma (total 24 patients)	7	29.1	5	20.8	1	4.1	0	
Group III								
Giant cell carcinoma (total 9 patients)	2	22.2	1	11.1	0		0	
Small cell carcinoma (total 30 patients)	6	20.2	2	6.6	0		0	

roid to date depends upon surgery, and this surgery, to accomplish the best results, must be radical. In those cases that are infiltrative it is impossible to remove all of the growth, so dependence must be placed upon some sort of radiation therapy. In the series presented, postoperative roentgen treatment as shown in Table v was used. In those cases of residual adenocarcinoma localized or with persistent fixed glands, radium treatment, as outlined, is advisable.

RESULTS

The results of the ten to twenty year treatment for each group are listed in Table vi and, with the treatment outlined, the life expectancy of the various types of tumors is indicated.

SUMMARY

Thyroid cancers arise in pre-existing tumors.

The clinical evaluation of an individual case does not exclude cancer.

Single thyroid nodules are malignant in 10 per cent of the patients coming to operation.

We believe radical surgery followed by roentgen therapy is the treatment of choice with the exception of alveolar adenomas, malignant, which we do not believe are clinically malignant.

A tumor dose of 4,800 to 6,000 roentgens is necessary to control the growth of papillary adenocystoma with invasion, papillary adenocarcinoma, and small cell carcinoma. (Giant cell carcinoma does not respond to doses of roentgen radiation as outlined here.)

Radium is a useful adjuvant in the treatment of residual and infiltrative tumors, especially alveolar adenocarcinoma. An attempt should be made to give at least 6,000 gamma roentgens to the periphery of the tumor.

Ten to twenty year follow-up studies show that good results have been obtained in the treatment of the following: (*a*) alveolar adenomas with malignant change; (*b*) papillary adenocystoma with invasion, and (*c*) papillary adenocarcinoma. Poor results are obtained in the treatment of alveolar adenocarcinoma and giant cell carcinoma. The failure of treatment of the small cell type of cancer of the thyroid is usually a result of its widespread infiltration at the time the patient comes for treatment.

Associated hyperthyroidism is rare in thyroid cancer, occurring in approximately 8 per cent.

Radioactive iodine will probably prove of value in the more slowly growing types. According to our experience there is no reason to use it in primary alveolar adenoma with invasion since the results of surgery alone are satisfactory. In the papillary adenocystomas, malignant, and the papillary adenocarcinomas it should be of definite value. It should be tried in the alveolar type but since many of the cells of this type may be more anaplastic, other types of radiation should be employed.

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DISCUSSION

Dr. William E. Howes, Brooklyn, New York. Such a long term review of results allows us a double advantage: first, to study the natural course of the disease, and second, it gives us some insight into the efficiency of our treatment. Actually the percentage of the survivors shown closely parallels the histopathologic rating in that cases with the more mature tumors, such as the fetal adenoma with invasion, the papillary cystadenoma, and the papillary adenocarcinomas have by far the greater chance of survival. The authors have shown that the fetal adenoma with malignant change may be easily eradicated by proper surgical removal. This may be likened somewhat to the adenoma malignum which arises in the endometrium and which has on occasions been eradicated by curettage alone. Nevertheless, either lesion left in situ and not treated will progress and finally kill.

I agree with Dr. Hare that the papillary cystadenoma and the papillary cystadenocarcinoma could be grouped into a single listing, as they closely parallel each other, both as to

their microscopic appearance as well as their tendency to spread both by local invasion and to metastasize to the adjacent cervical lymphatics, thus differing from the alveolar adenocarcinoma which is so prone to metastasize to long bones and viscera. Furthermore, the papillary carcinomas are particularly sensitive to irradiation. Treatment, therefore, should consist of thyroidectomy, including radical neck resection and postoperative irradiation.

Dr. Hare has shown by delivering a tumor dose of close to 6,000 r that the progress of disease may be inhibited for many years, and that if the tumor does not entirely disappear, at least 65 to 80 per cent of the patients will survive five years and close to that percentage will survive ten years. The author admits the difficulty encountered in attempting to eradicate the alveolar adenocarcinoma and the anaplastic carcinoma. Unfortunately, but few of these latter groups have any avidity for radioiodine and thus treatment would appear to be futile. This, however, has not been my personal experience in that I have found that patients have experienced some added relief of pain arising in bone metastases within a few hours after a therapeutic dose of radioiodine; this, in spite of there being no measurable amount of iodine collected within these metastases. We had one very interesting case in this respect in which a patient received two therapeutic doses of radioiodine and was recently re-operated upon to remove any residual thyroid tissue, and on operation the surgeon and we were shocked to note that we were unable to find the slightest remnant of thyroid gland remaining. This patient showed no evidence of hypothyroidism—there must have been some active thyroid tissue present—and thus I infer that that must have been present in the metastases.

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SOME RESULTS FROM THE USE OF RADIOACTIVE IODINE, I^{131}, IN THE DIAGNOSIS AND TREATMENT OF TOXIC GOITER*†

By SIDNEY C. WERNER, M.D., LAWRENCE D. GOODWIN, M.D., EDITH H. QUIMBY, PH.D., *and* CHARLOTTE SCHMIDT, B.A.

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THE present report concerns the clinical use of radioiodine at the Presbyterian Hospital, New York, and is based upon data from two distinct lines of investigation. First, the uptake of radioiodine by the thyroid gland has been studied as a potential exclusion test for hyperthyroidism.[7] Second, I^{131} has been employed as an agent in the treatment of hyperthyroidism.[8]

The eight day half-life isotope of iodine, I^{131}, became available from Oak Ridge three years ago. Treatment of toxic goiter with radioiodine was begun in this clinic at that time,[9] and concurrently a diagnostic study was begun with tracer doses of I^{131} to assess thyroid activity in man.[10] In the past year, the latter investigation was extended to compare the accuracy and suitability of the radioiodine tracer technique with that of the basal metabolism test, in routine clinical use.

The determination of basal metabolism as done routinely is subject to many limitations. Excitement or emotion may negate the value of the test since inability to relax and increased muscular tonus or involuntary motions frequently accompany nervous tension. The patient is no longer in a "resting" state and an increase in oxygen consumption may reflect only the added requirements of muscular activity rather than increased basal requirements. Involuntary variations in the expiratory position of the thoracic cage also may result from emotion during the test, with consequent invalid results. Muscular exertion just before or during the test, inadvertent smoking, or eating prior to the examination, fever, and dyspnea due to heart or pulmonary failure may lead to erroneous values. Sighing and other respiratory variations may make it impossible to estimate accurately oxygen consumption from the spirogram. Finally, there are many disorders such as hypertensive disease, leukemia or lymphomata, and chromaffinoma of the adrenal, in which the basal metabolic rate may be elevated as part of the disorder, unrelated to an underlying increase in thyroid function.

Accordingly, it has long been recognized that it would be advantageous to have a test which has less overlap with the findings in other clinical states and which is less influenced by subjective factors. The determination of radioiodine uptake by the thyroid gland appears to provide such a test, and overcomes many of the objections to the basal metabolism procedure. The method is objective. It does not require preceding rest and fasting. The results show much less overlap with those found in diseases other than those of the thyroid. The experiment set up at the Presbyterian Hospital to appraise the tracer technique as a routine procedure was designed to compare the concurrently determined tracer uptake and basal metabolic rate. All ward patients for whom a basal metabolism test was ordered were given a tracer dose of I^{131} as well, in a routine manner and with no special precautions to insure extreme accuracy. For the tracer test, 40 microcuries of I^{131} were administered by mouth. Uptake

* From the Departments of Medicine and Radiology, College of Physicians and Surgeons, Columbia University and the Presbyterian Hospital in the City of New York. Presented at the Thirty-first Annual Meeting, American Radium Society, Atlantic City, N. J., June 5–7, 1949.

† This investigation was supported (in part) by a research grant from the Division of Research Grants and Fellowships of the National Institute of Health, United States Public Health Service.

was measured directly over the thyroid twenty-four hours later, according to previously established methods.[9] The results of both tests were subsequently compared with the final diagnosis of the state of thyroid function, and unexpected difficulties or sources of error, and the technical simplicity of both procedures, were noted.

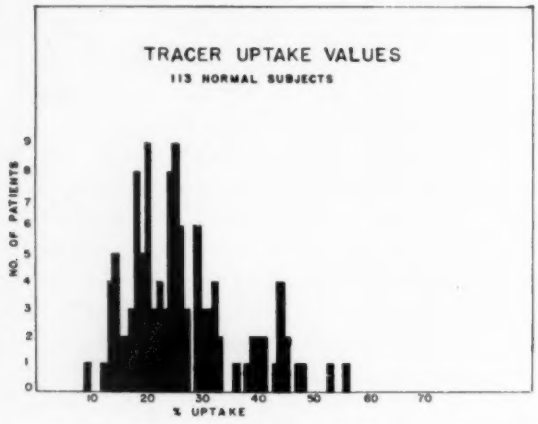

FIG. 1. Block diagram showing distribution of percentage uptake of radioactive iodine in 113 euthyroid individuals.

One hundred seventy-five patients were tested, of whom 113 ultimately were shown to be euthyroid. A diagnosis of either hyperthyroidism, hypothyroidism or some other thyroid disorder was made in the others. The values for radioiodine tracer uptake and basal metabolic rate of the 113 euthyroid patients are presented. In Figures 1 and 2 are shown block diagrams of the distribution of percentage uptake of radioiodine, and the values of the basal metabolic rate respectively.* Scatter diagrams, shown in Figures 3 and 4, indicate the distribution of cases which fall outside the accepted "normal limits." From previous study of a larger series of cases, the normal radioiodine uptake at twenty-four hours has been established as between 10 and 35** per cent.[10] In Figure 3, those euthyroid subjects in this series, whose uptakes fell outside this range, are plotted with respect to the basal metabolic rate. Sixteen per cent of the patients had uptakes greater than 35 per cent; with 2 exceptions these had normal or subnormal basal metabolic rates. In addition, 1 patient's uptake was just below the normal range, making a total of 17 per cent outside the normal limits.

The normal range for the basal metabolic rate is usually accepted as ±10 per cent. In Figure 4 are plotted the euthyroid individuals whose values fell outside this range, with their radioiodine uptake values. Twenty-eight per cent of the patients have basal metabolism values outside the usual limits. Of these 32 patients, 12 values are high and 20 low. Of the high values, all but 2 had normal iodine uptakes, while of the low ones, 5 show higher than normal iodine readings. The explanation for this is not at hand.

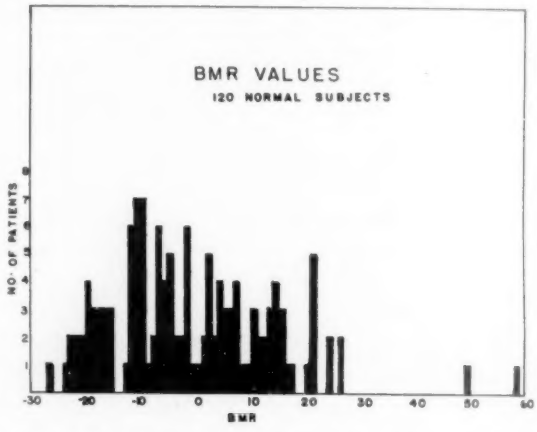

FIG. 2. Block diagram showing distribution of basal metabolic rate values among 120 euthyroid individuals.

It should be pointed out that the results from basal metabolic rate determination of the slightly larger series indicated in Figure 2 show a somewhat higher incidence (38 per cent) of values in excess of ±10 per cent than is shown in Figure 4. However, this series is weighted by repeated determinations on subjects who did not show normal values in the first test.

* The block diagrams include for the basal metabolic rate 7 additional cases in whom tracer values were inaccurate because of previous iodine administration, and also 14 results from repetition of the basal metabolic rate determination in some of the other 113 subjects.

** More recently, 40 per cent uptake has been used as the normal upper limit.

From the data of a separate study of radioiodine uptake in hyperthyroidism, involving a total of 302 patients, the percentage of values in the toxic group which fall within the normal range of uptake has been determined. Six per cent of patients with toxic goiter show uptakes less than 35 per cent at twenty-four hours. The overlap of basal metabolism readings between this group and normal subjects, values between +10 per cent and +20 per cent, has not been worked out accurately. It is at least as great, if not greater, than the overlap seen with radioiodine tracers.

It is frequently necessary to repeat basal metabolism tests to rule out emotional effects. This is unnecessary with the tracer test with which the need for repetition is rare. However, errors in the tracer test do occur. For example, uptake may be arrested as a result of preceding stable iodine administration, whether given as Lugol's solution or in organic form in the dyes used for cholecystography and intravenous pyelography. Similarly, the ingestion of thyroid medication or of antithyroid drugs before the tracer test may also inhibit iodine uptake. As much as twelve weeks may have to elapse before the function of iodine uptake is resumed. Another source of error may result from therapy for toxic goiter, such as with operation or radioiodine. These measures may disrupt the direct correlation which normally exists between the functions of iodine uptake and thyroid hormone secretion. A careful history and physical examination should avoid the above pitfalls.

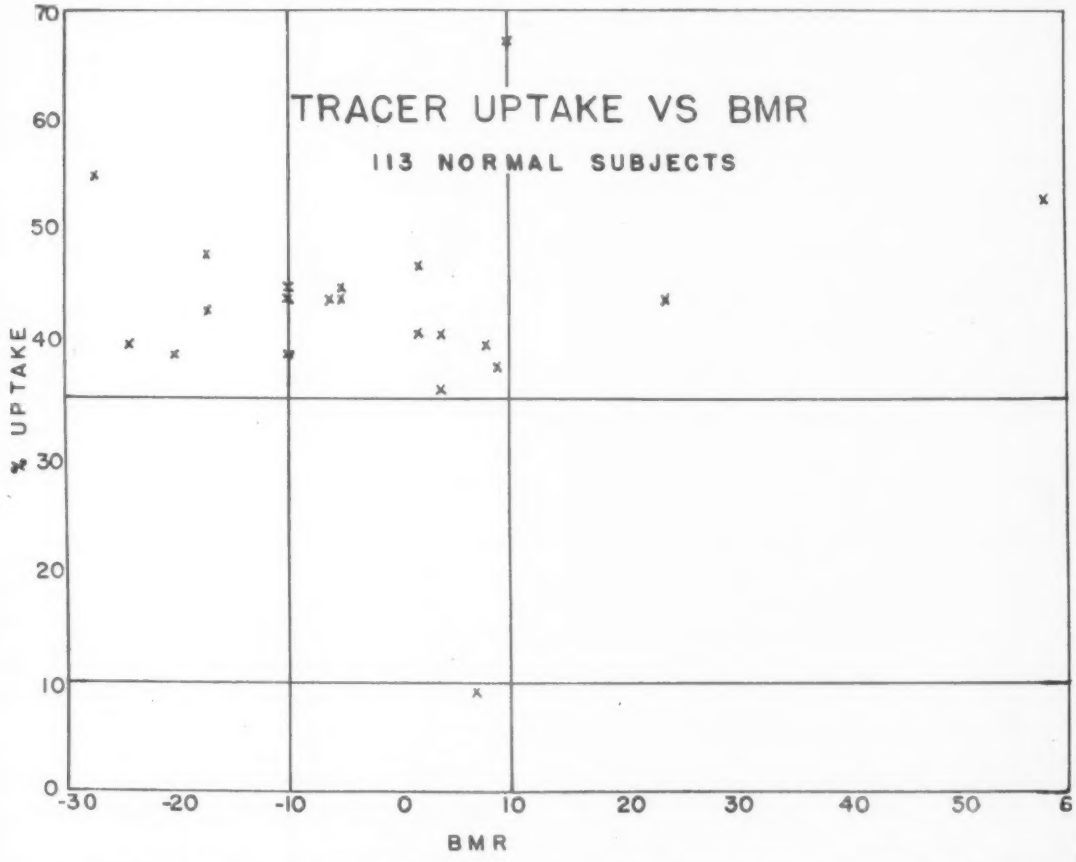

FIG. 3. Scatter diagrams showing distribution of basal metabolic rate values in 20 euthyroid individuals whose radioiodine uptakes were outside normal limits.

It is evident then that the tracer technique with radioiodine is useful as an estimate of thyroid function but is subject to error and presents certain irregularities. However, its accuracy is considerably greater than that of the basal metabolism, it has greater simplicity, is more acceptable to the patient and requires less cooperation from the patient. It seems not unlikely that the tracer test will be used as the method of first approximation of thyroid function, instead of the basal metabolism as at present. This usage would be similar to that of the exclusion test for syphilis. Abnormal values in the tracer test, or sharp discrepancies from the clinical impression would then call for confirmation by the basal metabolism and other procedures. In this way, 85 per cent or more of problems would be screened out and only 15 per cent would be left for more detailed and laborious confirmatory procedures, such as modifications of the simple tracer technique above [2,3,4,5,6] and the chemical determination of serum iodine.[1]

The results from the therapeutic use of radioiodine, I^{131}, also are of interest. One hundred and three cases have been treated in the past three years. The efficacy of a relatively constant dose of 3–4 mc. I^{131} was first observed from the initiation of the study until January, 1948, and has been presented elsewhere. The fact that patients with high toxicity and large glands received relatively little total radiation by this method, and were preponderant in the failures, led to the use of a wider range of dosage, from 3 to 6.5 mc. I^{131} after January, 1948. Since then, there have been treated 63 patients with frank toxic

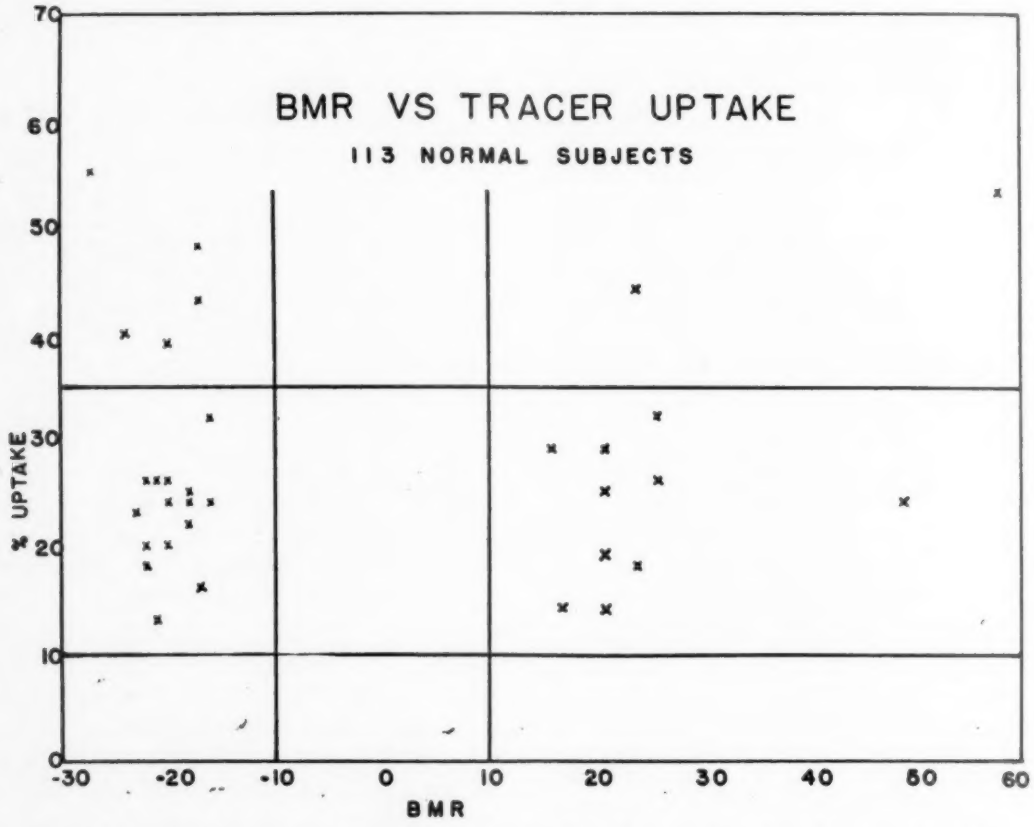

FIG. 4. Scatter diagram showing distribution of radioiodine uptake values for 32 euthyroid individuals whose basal metabolic rates were outside normal values.

goiter. The dosage level planned for in this group has been 100 μc. per estimated gram of gland weight. Forty-four of these had primary unoperated toxic goiter, while toxic goiter was recurrent after operation in 19. Follow-up has been at least four months and extends to one and one-half years. Following a single dose of I^{131}, 36 of the 63 patients in the later series (59 per cent) were brought into remission and 5 per cent were made hypothyroid. A second dose administered to the failures at four months or later after the initial therapy brought the total in remission to 81.3 per cent, while 6 per cent now had hypothyroidism. A final third dose was given to those not yet in remission four months or more after the second treatment. The final total in remission following this dosage was 90 per cent, while 4 patients, or 6.9 per cent, were now apparently permanently hypothyroid. Thus 96.5 per cent of the group were relieved of toxicity of hyperthyroidism or were made hypothyroid and only 3 per cent represented failure of therapy and were treated surgically. Complications after I^{131} therapy, other than hypothyroidism, were negligible except for the onset of malignant exophthalmos without progression in 2 patients, and a flare-up in toxicity with cardiac repercussions in 1 patient.

Certain drawbacks of radioiodine therapy for toxic goiter are evident. Thus, the lag of two to three months before remission is induced, a delay which may not be tolerated in severe thyrotoxicosis, is a definite handicap. Also, the risk of delay may be still further increased, since only 2 out of 3 patients respond to an initial dose of I^{131}. However, these handicaps are not too serious and a way may be found to control toxicty during the period until radioiodine induces a remission.

One major difficulty stands in the way of general acceptance of internal radiation therapy, namely, fear of later malignant change as a consequence. The collection of radioiodine by the thyroid gland is not symmetrical throughout the gland. Thus some cells may receive an intense irradiation. This has led some workers to feel that cancer of the thyroid after the lapse of some twenty years is not unlikely. This problem remains, and will probably be settled only by the passage of time. It should be mentioned that such late malignant change has not followed external radiation therapy.

At present, the following indications for therapy in toxic goiter have been established. First, the success of I^{131} in *recurrent* toxic goiter as opposed to other available methods of therapy has resulted in the almost exclusive use of radioiodine in this and other clinics, despite the theoretical possibility of neoplasia. Also, the complicated patient unsuited for surgery, and the patient with primary toxic goiter over the age of forty-five in whom late malignancy is not too serious a problem increasingly have come to be considered as presenting indications for this method of treatment, instead of the other modalities.

SUMMARY

1. The results are presented of a study in 175 hospital patients, to compare the radioactive iodine tracer technique with the basal metabolism test in routine clinical use. It is suggested that the tracer technique provides an exclusion test for thyroid dysfunction of greater objectivity and accuracy than the basal metabolism.

2. The results of treatment of hyperthyroidism with radioiodine, I^{131}, in 103 patients, are summarized. A very high remission rate (90 per cent) has been obtained. The complications and disadvantages are discussed.

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REFERENCES

1. Barker, S. B. Determination of protein bound iodine. *J. Biol. Chem.*, 1948, *173*, 715.
2. Clark, D. E., Moe, R. H., and Adams, E. E. Rate of conversion of administered inorganic radioactive iodine into protein bound iodine of plasma as aid in evaluation of thyroid function. *Surgery*, 1949, *26*, 331.

3. McCONAHEY, W. F., KEATING, F. R., and POWER, M. H. Behavior of radioiodine in blood. *J. Clin. Investigation*, 1949, *28*, 191.
4. MYANT, N. B., POCHIN, E. E., and GOLDIE, E. A. G. Plasma iodide clearance rate of human thyroid. *Clin. Sc.*, 1949, *8*, 103.
5. STANLEY, M. M., and ASTWOOD, E. B. Determination of relative activities of antithyroid compounds in man using radioactive iodine. *Endocrinology*, 1947, *41*, 66–84.
6. TAUROG, A., and CHAIKOFF, I. L. Metabolic interrelations of thyroxine and diiodotyrosine in thyroid gland as shown by study of their specific activity-time relations in rats injected with radioactive iodine. *J. Biol. Chem.*, 1947, *169*, 49–56.
7. WERNER, S. C., GOODWIN, L. D., and QUIMBY, EDITH H. Tracer technique with radioiodine I^{131} as potential substitute for basal metabolic rate determination in routine clinical practise. *J. Clin. Endocrinol.*, 1949, *9*, 664.
8. WERNER, S. C., QUIMBY, EDITH H., and SCHMIDT, CHARLOTTE. Radioactive iodine, I^{131}, in treatment of hyperthyroidism. *Am. J. Med.*, 1949, *7*, 731.
9. WERNER, S. C., QUIMBY, EDITH H., and SCHMIDT, CHARLOTTE. Clinical experience in diagnosis and treatment of thyroid disorders with radioactive iodine, (eight-day half-life). *Radiology*, 1948, *51*, 564–578.
10. WERNER, S. C., QUIMBY, EDITH H., and SCHMIDT, CHARLOTTE. Use of tracer doses of radioactive iodine, I^{131}, in study of normal and disordered thyroid function in man. *J. Clin. Endocrinol.*, 1949, *9*, 342.

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CLINICAL COURSE OF TWO HUNDRED CASES OF ANGINA PECTORIS TREATED WITH ROENTGEN IRRADIATION OF THE ADRENALS (1937–1947)*

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THE rationale and technique of roentgen treatment over the adrenal glands for angina pectoris has been discussed in detail in previous publications.[15,18,19,21] The procedure is intended to decrease the abnormal excretory irritability of the adrenal medulla which had been found to be a characteristic of angina patients.[19]† These adrenal medullary discharges are believed to lead to acute painful anoxia of the heart muscle whose coronary arteries are incapable of adequate dilatation whenever an anoxia-producing influx of epinephrine into the myocardium takes place, as during physical effort, emotions, exposure to cold[23] and similar situations, accompanied by stimulation of the adrenosympathetic neurosecretory system.

Since the specific, chemically anoxia-producing effect of epinephrine as well as of locally discharged sympathin upon the myocardium, regardless of the volume of coronary blood flow, has become recognized in its fundamental significance for heart metabolism and function,[1,4,5,6,23] it is no longer necessary to try to interpret the anginal syndrome entirely in terms of purely mechanistic conceptions, such as a "coronary spasm" or a discrepancy between coronary flow and myocardial dynamic performance, particularly as the latter is often not demonstrable during the anginal attack.[17]

The seemingly strongest argument against the concept of an essentially biochemical mechanism of the anginal syndrome, namely the usually prompt relief through a supposedly purely vasodilator drug (nitroglycerin), does not seem tenable in the light of newer observations[22,24] which suggest that nitroglycerin acts not only upon the coronary artery muscles as a dilator but also on the heart muscle itself as a direct antagonist against epinephrine- and sympathin- (arterenol-) induced functional and electrocardiographic effects.

Beginning in 1937, two hundred patients suffering from angina pectoris on effort were given roentgen treatments over the adrenal glands under the author's medical supervision. In addition to the adrenal treatments, roentgen irradiation over the upper thoracic and cervical spine was also given to 57 of these patients in consideration of the frequent association of true coronary angina with osteoarthritis of the spine and with thoracic "sympathicoganglionitis."[16] In cases of this kind, an exaggerated anoxiating neurosecretory activity of the cardiac sympathetic fibers can be assumed to contribute to myocardial anoxia through the biochemical action of sympathin.

In confirmation of earlier reports,[18,23] a beneficial effect of roentgen treatment of the adrenal glands in angina pectoris has been described by several European investigators.[7,8,11,13,26] In this country only slight attention has been paid to it so far, except for the mentioning of favorable experiences by Hutton and Fahlstrom[10] and Scherf and Boyd,[25] and a detailed report on 23 cases of severe angina pectoris treated by McMillan and Rousseau.[15] These authors obtained "marked relief" in 74 per cent of their patients, a percentage well in agreement with that previously described by the writer.[18,23]

In order to gain information on the long-range effect of the therapeutic roent-

† The opinion expressed in this article,[19] that the colorimetric results obtained included adrenal cortical steroids, had to be abandoned when it was found that such steroids do not participate and that the readings are essentially due to the presence of sympathomimetic amines (epinephrine and sympathin) (see Raab, W., *Biochem. J.*, 1943, *37*, 470).

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TABLE I

DEGREES OF SEVERITY AND OF IMPROVEMENT AMONG 200 CASES OF ANGINA PECTORIS TREATED WITH ROENTGEN IRRADIATION OF THE ADRENALS (57 OF THEM IN COMBINATION WITH IRRADIATION OF THE UPPER THORACIC AND CERVICAL SPINE)

Degree of severity	Cases per cent of total	Degree of improvement	Cases per cent of total	
Severe	36	+++	31	76%
Medium	52	++	30	
Light	12	+	15	
		−	24	

gen procedures under consideration, questionnaires were repeatedly sent out to the treated patients, including 100 patients abroad, who had been treated in Vienna in 1937 and 1938. As was to be expected, this latter group proved greatly depleted through displacement, death due to air bombardments and other violence, besides the instances of natural death. Personal answers were recently received from 23 out of the 100 European patients, while, on the other hand, 19 out of 100 patients treated in Burlington from 1937 to 1947 failed to answer the last inquiry early in 1948. Thus, a final clinical follow-up to date was not possible in 48 per cent of the cases. The mere fact of death, without details regarding the clinical condition preceding death, was reported in 12 per cent of all cases.

In the following tabulations the cases were subdivided according to severity (severe, medium, light) considering both intensity and number of attacks, and according to the degree of subjective improvement, reported subsequent to treatment (Table I). Such improvements were listed as probably connected with the roentgen therapy if they occurred within a limited period of time following the latter. The longest interval was fourteen weeks, while in the great majority it was much shorter (total average four weeks, see Table II) in apparent analogy to the several weeks' period elapsing between experimental high-dosage roentgen irradiation of the adrenals in animals and the onset of a resulting secretory depression.[20] Improvements were included in the tabulation only if they lasted for at least two months without interruption (Table II). They were classified as +++ (complete or almost complete disappearance of anginal symptoms), ++ (considerable diminution of symptoms), + (slight improvement) and − (no improvement).

TABLE II

Degree of improvement.	No. of cases	Period of follow-up (mo. av.)	Overall duration of improvement (mo.)		Approximate interval between roentgen treatment and onset of maximum improvement (weeks)		Reported interruption of improvement. Cases per cent per group	Reported complete permanent relapses. Cases per cent per group	Reported nonfatal myocardial infarctions after roentgen treatment	
			Range	Average	Range	Average			Cases per cent per group	Interval (mo. av.)
+++	63	52	6–135	43	1–12	4	10	13*	6*	44
++	60	35	3–126	24	1–14	4	7	27*	8*	28
+	29	29	2–127	18	1–12	5	17	38*	3*	52
−	48	11	—	—	—	—	—	—	2*	5
Total	200	41	2–135	31	1–14	4	10	23*	6*	34

* These percentages were calculated in relation to the number of cases of each respective group. These include a total of 96 cases about the clinical condition of which no adequate up-to-date details were available. Consequently, the figures are, without doubt, too low. They are intended only to illustrate the approximate proportions from group to group.

As shown in Table I, more than one-half of all patients belonged in the category of medium severity, 36 per cent were severe. Taking all degrees of improvement into account, a total of 76 per cent of all cases showed at least some improvement for an average period of thirty-one months. Thirty-one per cent became entirely or almost entirely free of symptoms for an average of forty-three months, beginning on an average four weeks following the respective series of treatments (Table I) and 30 per cent were considerably improved for an average of twenty-four months, beginning after an analogous interval. Thus, the most complete clinical improvements were also the longest lasting ones, as a rule.

More or less intense transitory relapses, some of which were again abolished by renewed roentgen treatment, occurred in a small minority of cases (10 per cent of the total), while complete and apparently permanent relapses were reported in 23 per cent of all cases (Table II). In 13 such cases renewed roentgen treatment was undertaken and proved unsuccessful.

Table III shows the number of roentgen series applied over the adrenals in relation to the degrees of improvement achieved. Thirty-eight per cent of all patients received only one series, which proved sufficient in more than one-half of the best responding cases, while in the less readily responding cases more treatments had to be given. In the non-responsive group, the number of treatments would have been greater and the results probably somewhat better if the patients had not become discouraged and had not failed to come for further therapy. Nevertheless, even four series of irradiations did not further improve the results in some of the not maximally responding cases.

Cervical and thoracic roentgen treatments were given in addition to the adrenal irradiations in 28 per cent of all patients. No clear impression as to the relative merits of this combined treatment, as compared with plain adrenal irradiation, has yet been gained. Four-fifths of the +++ improvement group and two-thirds each of all the other groups had been treated over the adrenals alone.

The occurrence, after an average interval of thirty-four months, of non-fatal myocardial infarctions in patients previously treated with roentgen rays was reported in 6 per cent of all cases (Table II). The seemingly low incidence of only 2 per cent in the patients who had not responded to treatment is undoubtedly due to the short average period (eleven months) during which information on the clinical course of these cases was available. Taking the follow-up time into account, the occurrence of non-fatal myocardial infarction did not differ greatly among the improved groups (Table II).

The total number of reported deaths (Table IV) amounted to 32 per cent of all cases. Nine per cent were diagnosed cardiac deaths and the others were composed of

Table III

Degree of improvement	Number of adrenal irradiation series (per cent per group)*				Number (per cent) of cases treated with irradiation over the spine	Number of series per capita	
	1 series	2 series	3 series	4 series		Adrenal	Spine
+++	52	34	14	0	19	1.6	0.2
++	26	39	28	7	33	2.1	0.5
+	24	34	32	10	31	2.3	0.4
−	43	39	16	2	31	1.8	0.4
Total	38	37	21	4	28	1.9	0.3

* A total of 69 roentgen series over the spine was given to 57 patients.

TABLE IV

Degree of improvement	No. of cases	Reported cardiac deaths			Reported non-cardiac and undefined deaths. Cases per cent per group
		Cases per cent per group	Interval (mo.)		
			Range	Average	
+++	63	10	7–96	59	21
++	60	13	6–73	34	25
+	29	7	34–36	35	24
−	48	6	6–71	39	21
Total	200	9	6–96	42	22

definitely non-cardiac deaths through disease or violence, and of deaths of an unidentified nature. The percentage of combined cardiac and other deaths was relatively low in the +++ improvement group and relatively high in the non-improved group, considering the respective lengths of follow-up periods. Four deaths which occurred within the first month after the first treatment were not included in the statistical survey.

The average number of years elapsed between the onset of anginal symptoms and the date of the last information received or of death (Table v) was at least 7.2 years for all 200 patients, at least 7.4 years for those still alive at that time (137 cases), and 6.6 years for the dead (63 cases). This latter figure compares favorably with older statistics for the duration of angina pectoris to death by Herrick and Nuzum[9] (3 years, 50 cases), Mackenzie[14] (5.4 years, 214 cases), White[27] (3.4 years, 66 cases), White and Bland[28] (4.4 years, 213 cases), Eppinger and Levine[3] (4.6 years, 141 cases), especially since death had been precipitated prematurely in a considerable number of the European patients included in the present roentgen irradiated series. However, in a large long-range observation series (497 cases, 1920–1943) by White, Bland and Miskall[29] in which the percentage of deaths was 89, the average duration to death was 7.9 years, the average duration of the disease in those still living was 18.4 years and the average duration for the combined dead and living was 9.0 years. Thus, no definite claim can be made for a generally life-prolonging effect of roentgen treatment in angina pectoris cases.

TABLE V

AVERAGE NUMBER OF YEARS ELAPSED BETWEEN ONSET OF ANGINAL SYMPTOMS AND DATE OF LAST INFORMATION RECEIVED

	Number of cases	Average number of years
All cases	200	7.2
Alive when last information received	137	7.4
Dead	63	6.6
Patients (alive and dead) who had a myocardial infarction at any time during their illness	56	7.6

Strangely enough, the duration of the disease (Table v) in the 56 patients (combined alive and dead) who at any time before or after roentgen treatment had suffered one or more attacks of myocardial infarction, was at least 7.6 years, which is slightly more than that of the other 144 patients (7.0 years), and strikingly more than the average duration of the disease in 200 infarction cases (combined alive and dead), studied by Bland and White[2] (4.6 years), and 372 infarction cases of Levine and Rosenbaum[12] (2.6 years). Too much emphasis should not be placed on this point, as the cause of death was unknown in a comparatively large proportion of the

cases here considered, and the inclusion of all those actually due to myocardial infarction might have somewhat diminished the above mentioned average duration of the disease to death. Nevertheless, even under the fictional exaggerated assumption that all deaths were due to myocardial infarction, the average duration in all cases of diagnosed and imputed myocardial infarction combined would have been as long as 3.7 years. Hence, some degree of life prolongation in roentgen irradiated patients with a tendency to myocardial infarction seems to remain a possibility.

In an effort to find possible indications in regard to the prospect of success or failure of roentgen treatment, the data shown in Table VI were complied. They suggest that neither age nor blood pressure level nor tobacco smoking play any significant role in this respect. The severity of symptoms appeared to make a slight difference in that medium severe cases were prominent in each improvement group, while severe cases were most numerous among the failures. The presence of angina decubitus too seems to impair the outlook of therapeutic success somewhat but most important of all appears to be the duration of the disease before treatment is instituted; while its average ranged between 3.7 and 3.9 years in the responding groups, it was 6.2 years in the group of failures (Table VI). On the other hand, the incidence of myocardial infarctions as well as of pathological findings in the electrocardiograms was somewhat higher among the maximally improved cases than in any other group (Table VI).

The higher incidence of diagnosed osteoarthritis in the group of slight improvement, compared with the other groups of patients may be misleading, as roentgen examinations of the thoracic and cervical spine were carried out only sporadically, thus increasing the range of error. Syphilitic infection was too infrequent to permit any conclusions from the variations in its percentage among the four groups.

TABLE VI

Degree of improvement	No. of cases	Age av. yr.	Severity of symptoms. Per cent per group			Angina decubitus, per cent per group	Duration of symptoms before roentgen treatment (av. yr.)	Blood pressure, av.	Myocardial infarction before roentgen treatment		Ratio pathological to normal electrocardiograms per group*	Smokers, per cent per group	Osteoarthritis, per cent per group†	Syphilis, per cent per group
			Severe	Medium	Light				Cases, per cent of group	Time (av. mo.)				
+++	63	58	25	54	21	49	3.8	156/93	30	37	2:1	76	21	3
++	60	62	37	55	8	35	3.7	161/91	22	42	1.75:1	72	20	5
+	29	61	38	62	0	52	3.9	155/90	21	28	1:1	70	41	10
−	48	59	48	39	13	63	6.2	162/90	21	54	1.3:1	73	21	2
Total	200	60	36	52	12	49	4.4	159/91	24	41	1.5:1	71	24	5

* Electrocardiograms were taken in 129 cases before treatment.

† Roentgen findings of osteoarthritis of the upper thoracic and cervical spine were obtained in 48 cases.

COMMENT

In interpreting the clinical developments following roentgen therapy for angina pectoris, as represented in the above study, allowances must be made for diagnostic errors, incorrect reports by the patients and an inevitable arbitrariness in classifying the reported details. The possibility of some autosuggestive "imaginary" improvements exists. However, the fact that improvement hardly ever becomes noticeable during treatment and usually develops only after an interval of several weeks speaks against mere psychic suggestion. Its uninterrupted persistence in many of the European patients, despite severe mental and occasion-

ally also physical strain, fits into the same conception.

Objective evidence of a normalization of previously exaggerated adrenosympathetic discharges during exercise in clinically improved angina cases has been presented elsewhere.[23] In a limited number of patients in whom electrocardiograms, taken after the onset of clinical improvement, were available, a partial or complete disappearance of the depression of the ST interval and return of flat or inverted T waves to normal were observed both after exercise and at rest.[7,11,18]

Additional other treatments, given to some of the improved patients after roentgen irradiation, are not believed to have significantly influenced the statistically recorded data (purine derivatives in 10 cases, papaverin in 5, vitamin E in 3, testosterone in 2, strophanthin in 2, cytochrome C in 1). The use of nitroglycerin was continued, when needed.

The most important potential source of error in interpreting improvements after roentgen treatment appears to be the probability, stressed by White, Bland and Miskall[29] "that coronary heart disease, whether shown by the angina pectoris of temporary coronary insufficiency or by myocardial infarction with subsequent scarring, is actually in major part and in the majority of cases an acute or subacute rather than a chronic disease, though frequently with recurrence." While this factor may have played a part in some of the long range improvements here reported, it appears more than improbable that spontaneous disappearances of symptoms should have occurred with such frequency within a few weeks following roentgen treatment and that they should have been followed by such prolonged periods of freedom from symptoms as observed in a substantial number of the roentgen irradiated cases, (average 43 months in the 63 maximally improved patients).

The clear distinction between coronary disease and coronary heart disease has justly been emphasized as being of great significance[29] and deserves widest consideration. However, the author does not feel that the anginal ups and downs in patients with coronary sclerosis can be explained entirely on the basis of assumed anatomical changes in the coronary vascular bed (occlusions and establishment of collaterals) but rather that biochemical metabolic (neurohormonal) factors of adrenosympathogenic origin dominate the myocardial situation responsible for the anginal syndrome.

No untoward side-effects of the roentgen treatments were observed apart from some degree of nausea during a few days, occurring in about 15 per cent of all cases, and a transitory skin rash over the irradiated areas in one case.

SUMMARY

Two hundred patients with angina pectoris were treated between 1937 and 1947 with roentgen irradiation of the adrenals (57 of the cases also with irradiation of the cervical and upper thoracic spine).

Clinical improvement of all degrees, beginning on an average four weeks after the respective series of treatments and lasting for an average of thirty-one months, was reported by 152 patients; maximum improvement (complete or almost complete freedom from symptoms) was reported by 63, lasting for an average of forty-three months.

Complete permanent relapses were reported in 23 per cent, non-fatal myocardial infarctions in 6 per cent of the improved cases. Death (cardiac and other) occurred in 32 per cent of all cases and no indication of a life-prolonging effect of the treatments was obtained, except possibly in patients who had developed myocardial infarctions.

No definite clinical criteria for the prospect of therapeutic success could be statistically identified but cases of long standing and with angina decubitus seem somewhat more likely to fail to respond than others.

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REFERENCES

1. Barcroft, J., and Dixon, W. E. Gaseous metabolism of mammalian heart. Part 1. *J. Physiol.*, 1906–1907, *35*, 182–204.
2. Bland, E. F., and White, P. D. Coronary thrombosis (with myocardial infarction); ten years later. *J.A.M.A.*, 1941, *117*, 1171–1173.
3. Eppinger, E. C., and Levine, S. A. Angina pectoris; some clinical considerations, with special reference to prognosis. *Arch. Int. Med.*, 1934, *53*, 120–130.
4. Evans, C. L., and Ogawa, S. Effect of adrenalin on gaseous metabolism of isolated mammalian heart. *J. Physiol.*, 1914, *47*, 446–459.
5. Gollwitzer-Meier. K., Kramer, K., and Krüger, E. Die Wirkung des Adrenalins auf die Energetik des Herzens. *Arch. f. d. ges. Physiol.*, 1936, *237*, 639–650.
6. Gremels, H. Ueber die Steuerung der energetischen Vorgänge am Säugertierherzen. *Arch. f. exper. Path. u. Pharmakol.*, 1936, *182*, 1–54.
7. Hadorn, W. Untersuchungen des Herzens im hypoglykämischen Schock. *Arch. f. Kreislaufforsch.*, 1937, *2*, 70–156.
8. Hadorn, W. Behandlung der Angina pectoris. *Praxis*, 1937, *20*, 285.
9. Herrick, J. B., and Nuzum, R. F. Angina pectoris. *J.A.M.A.*, 1918, *70*, 67.
10. Hutton, J. H., and Fahlstrom, S. Syphilis, hypertension, and endocrines. *Urol. & Cutan. Rev.*, 1947, *51*, 203–205.
11. Kienle, F. Praktische Elektrokardiographie. Georg Thieme, Leipzig. 1944, p. 150.
12. Levine, S. A., and Rosenbaum, F. F. Prognostic value of various clinical and electrocardiographic features of acute myocardial infarction; ultimate prognosis. *Arch. Int. Med.*, 1941, *68*, 1215–1231.
13. Lippross, O. Zur Pathologie und Therapie der Angina pectoris. *München. med. Wchnschr.*, 1940, *87*, 727–730
14. MacKenzie, J. Angina Pectoris. Oxford University Press, New York, 1933.
15. McMillan, R. L., and Rousseau, J. P. Treatment of angina pectoris by irradiation of adrenal glands; clinical experience. *North Carolina M. J.*, 1946, *7*, 550–553.
16. Pletnev, D. D. Klinische Beobachtungen aus dem Gebiete des vegetativen Nervensystems; zur Theorie der Angina pectoris. *Ztschr. f. klin. Med.*, 1929, *109*, 603–612.
17. Raab, W. Angina pectoris simplex und hämodynamische Herzbelastung. *Ztschr. f. klin. Med.*, 1938, *134*, 595–603.
18. Raab, W. Roentgen treatment of adrenal glands in angina pectoris (100 cases). *Ann. Int. Med.*, 1940, *14*, 688–710.
19. Raab, W. Abnormal suprarenal discharges in angina pectoris and their control by x-ray therapy. J. *Clin. Endocrinol.*, 1941, *1*, 977–982.
20. Raab, W., and Soule, A. B., Jr. Effect of roentgen irradiation on hormone content and secretion of adrenal medulla. *Radiology*, 1943, *41*, 56–60.
21. Raab, W., and Soule, A. B., Jr. Rationale and results of roentgen treatment of adrenal glands in angina pectoris. Am. J. Roentgenol. & Rad. Therapy. 1944, *51*, 364–377.
22. Raab, W., and Humphreys, R. J. Drug action upon myocardial epinephrine-sympathin concentration and heart rate (nitroglycerine, papaverine, priscol, dibenamine hydrochloride). *J. Pharmacol. & Exper. Therap.*, 1947, *89*, 64–76.
23. Raab, W. Adreno-sympathogenic heart disease (neurohormonal factors in pathogenesis and treatment). *Ann. Int. Med.*, 1948, *28*, 1010–1039.
24. Raab, W., and Lepeschkin, E. Anti-adrenergic effect of nitroglycerine in the heart muscle. *Circulation* (in press).
25. Scherf, D., and Boyd, L. J. Cardiovascular Diseases. J. B. Lippincott Company, Philadelphia, 1947.
26. Schittenhelm, A. Aus dem Indikationsgebiet der Strahlenbehandlung von Hypophyse, Schilddrüse und Nebenniere. *Strahlentherapie*, 1939, *66*, 373–427.
27. White, P. D. Prognosis of angina pectoris and of coronary thrombosis. *J.A.M.A.*, 1926, *87*, 1525–1530.
28. White, P. D., and Bland, E. F. Further report on prognosis of angina pectoris and of coronary thrombosis. *Am. Heart. J.*, 1931, *7*, 1–14.
29. White, P. D., Bland, E. F., and Miskall, E. W. Prognosis of angina pectoris. *J.A.M.A.*, 1943. *123*, 801–804.

THE USE OF THE CINEFLUOROGRAPHIC METHOD FOR TEACHING PURPOSES

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ALTHOUGH the idea of cinefluorography is not new, its use has been limited by a number of factors, particularly the difficulty of obtaining a lens with sufficient speed to produce clear moving pictures of the fluorographic image at a reasonable rate of speed. In the past, this situation has been aggravated by the lack of screens of sufficient brightness and also by screen lag which tended to blur the image with resulting loss of detail. Within recent years most of these difficulties have been overcome. The cinefluorographic technique, which has been in regular use at this institution as a teaching method since 1941, has been used on occasion for a supplementary diagnostic technique and for fundamental research. It has developed so successfully that its regular utilization, particularly in teaching, should no longer be overlooked.

Probably the first major publication on this subject was that of Russell J. Reynolds[9] in May, 1928. With the inadequate roentgen apparatus and lenses of that day, he succeeded in making real progress toward practical cinefluorography, and his interest has been maintained continuously through the present time. In a publication in 1934, which was reprinted in this JOURNAL in 1935,[10] Reynolds makes the first known reference to the use of the Zeiss f. 0.85 lens which is, at this time, still the most satisfactory lens for this purpose. It is also of considerable interest that he called attention to the fact at that time that the focusing of the lens by means of a target illuminated with visible light can only be a first order approximation, since the effective focal length of the lens changes appreciably with the change in wavelength from ordinary white light to the illumination produced by either the deep blue-violet screen ("Fluorazure"), which was the first to be really successful in cinefluorography, or the more modern yellow-green fluorescent screens. Any significant change in the wavelength of the emitted visible light requires refocusing of the lens.

Janker[6] published illustrations of the mechanism of the human deglutition in 1936.

Using animation technique, Lewis Gregory Cole[2] produced a moving picture of gastric motility and showed it in Detroit in 1910. His subsequent work on the subject of gastric motility by cinematographic methods is too well known to require detailed discussion.

William H. Stewart, together with Ghiselin, and their associates [12,13] are already well known for their excellent work on study of the heart and motion of the diaphragm. Their pioneering work in the demonstration of interventricular septal defects has not yet been surpassed.

Barclay[1] and his associates in a complete publication in 1940 refer to probably the earliest of all references, the work of Macintyre[8] of Glasgow who made a successful roentgenographic motion picture of the movement of a frog's legs in 1897. In it Macintyre also describes for the first time the indirect (cinefluorographic) method, although obviously the equipment of that day was not practical for this purpose.

De Castro[4] has recently shown excellent detail studies and pointed out their usefulness as an aid to standard roentgen diagnosis.

An excellent review and bibliography of the entire subject is to be found in the work

of Jarre[7] who also personally contributed to the fundamental development of the cinefluorographic technique.

It is interesting to note, however, that in all cases from the very earliest to the present time, the same fundamental requirements with respect to the screen, the camera and the total exposure to the patient must be met.

The technical difficulties which must be overcome in order to accomplish the desired result of producing a clear film can be analyzed and at least a compromise solution to each can be reached without great difficulty. The first of these is the requirement for a very fast lens. In the Harper Hospital installation a Ziess f. 0.85 is used. The use of such a lens immediately produces the requirement for very precise focusing inasmuch as the depth of field of the lens is very shallow.

For the purposes of this paper we will

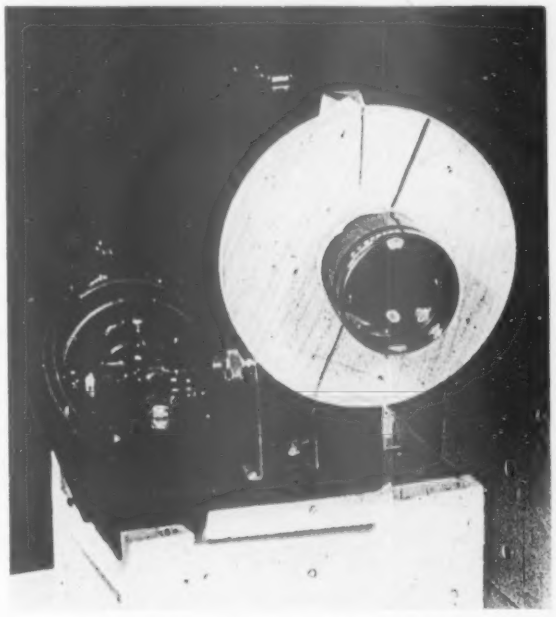

Fig. 1. Wooden focusing disc with logarithmic scale. Also shown is the electric motor drive on the side of the camera.

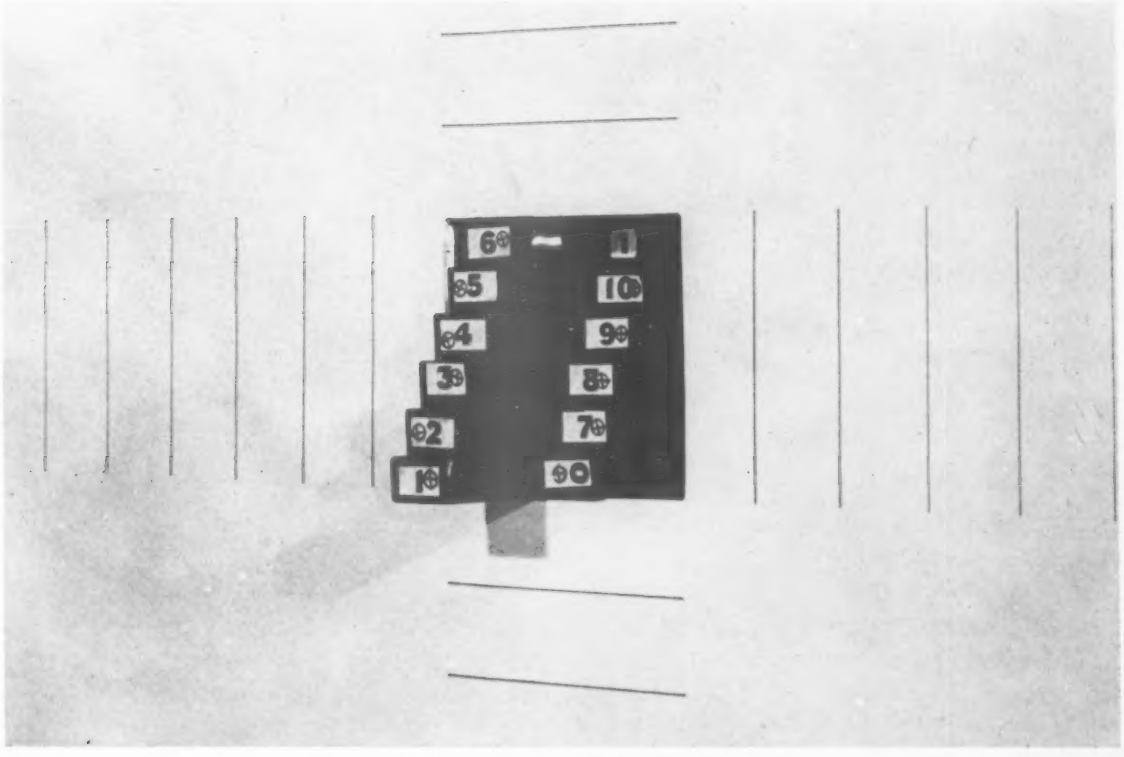

Fig. 2*A*. Central portion of the focusing target.

not go into the technical relationship between the allowable circle of confusion and depth of field. It can be shown, however, that for focal distances commonly used for cinefluorography from 18 inches to 6 feet between camera and screen, the theoretical depth of field will vary from 4 mm. to 120 mm. It was quickly found, however, that the theoretical depth of focus is of little practical use other than as a starting point.

The allowable error in setting the focal distance of the lens will be of the order of 15 microns. Even with the finest thread which is practical in the lens mount, the rotary displacement which can be tolerated, therefore, is very small. The simplest solution to this problem is to use a very large focusing ring on the lens mount.

The original focusing arrangement used on the Harper Hospital lens is shown in Figure 1 which shows the method of mounting the Zeiss lens on the modified cine-special camera built for us by Eastman Kodak Company.

FIG. 2*B*. Film strips showing focus and field coverage studies at 2½ feet and 5 feet 7½ inches.

This ring consisted of a piece of wood cut in the form of a disc and fastened to the focusing ring of the lens by a simple pressure screw. The peripheral surface of the wooden disc was covered with graph paper with a logarithmic scale and a simple pointer was mounted to index against the paper scale. The focal length could then be

set approximately and, by means of trial and error technique, the exact focal position for the lens for any given distance actual scale did not exactly conform to any theoretical scale when finished. However, by focusing against a paper target which

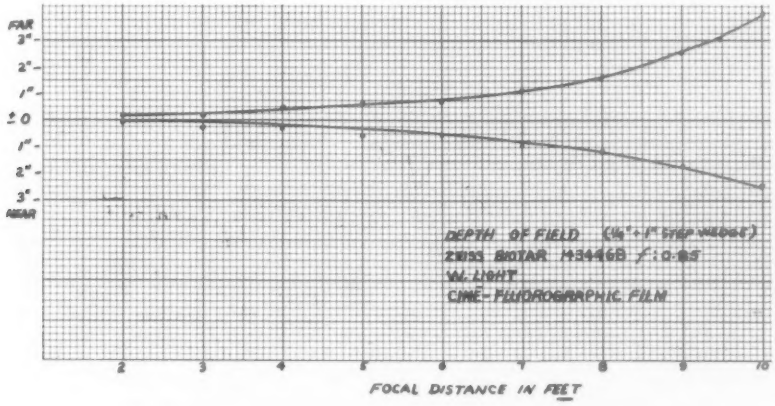

Fig. 3*A*. Depth of field from step wedge measurement.

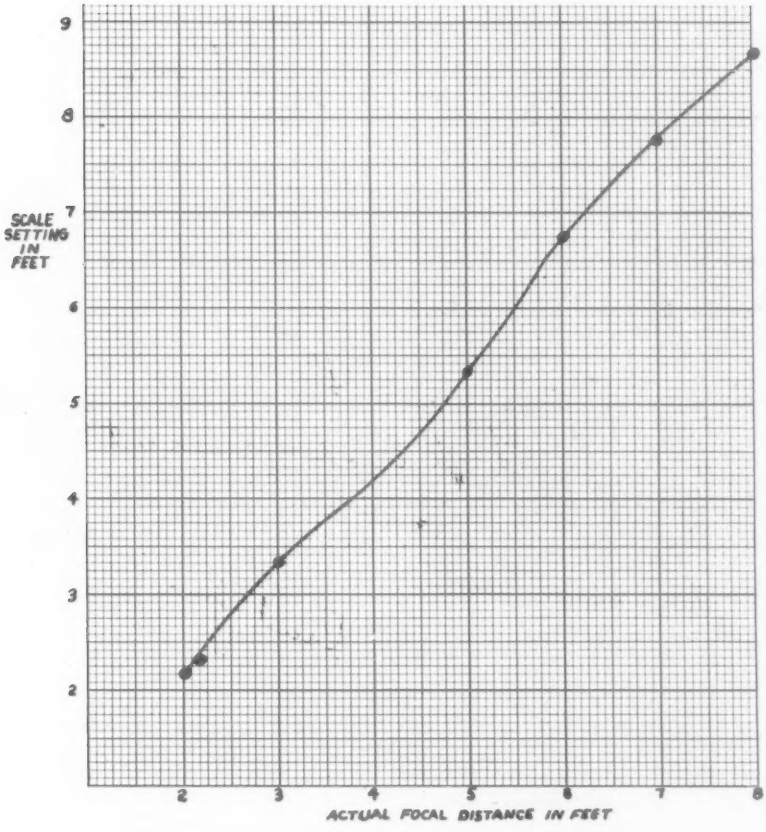

Fig. 3*B*. Scale setting versus actual distance.

could be plotted and tabulated. The most minor imperfections in the screw assumed significant proportions and, as a result, the showed three things, the area covered, the resolution throughout the area, and the depth of field actually recorded, a very pre-

cise scale was finally constructed.

The actual target used is shown in Figure 2*A* and two film strips resulting from exposure of this target are shown in Figure 2*B*.

The target consists of a flat piece of board faced with white paper and having ruled lines on its surface. A square hole is cut out of the center and a small step wedge with $\frac{1}{4}$ inch steps is mounted in the hole in such a position that the step numbered zero is on the plane of the paper. The camera on its permanent mount is then set on a simple wooden track in front of the target and a series of exposures is made for each desired distance. The resulting films are studied with a low power microscope. The first criterion is uniformity of focus throughout the area of the frame and, when this is obtained, the width of the image line resulting is measured and compared to the theoretical to determine the best focus. At this point a simple reading of the step wedge gives the depth of field for each camera distance. In actual fact, the depth of field determination later proved to be of only academic interest and for each camera distance there is only one focal setting which will give a satisfactory film. For the interest of anyone who may care to repeat the work, however, our results as to depth of field from 2 feet to 10 feet are shown in Figure 3*A*.

The best scale setting compared to the actual focal distance is shown in Figure 3*B* and the field coverage of the lens is shown in Figure 3*C*.

When this work was completed, the camera was returned to the factory and a permanent focusing ring of aluminum with the finished scale engraved on its periphery was built. The scale and pointer arrangement includes a locking screw for holding

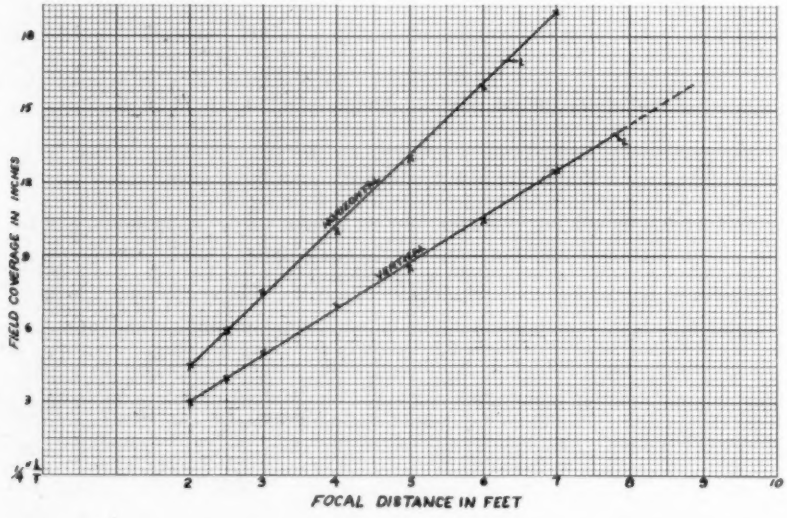

FIG. 3*C*. Field coverage for uniform resolution throughout field. "L" indicates limit of usable area of screen.

the focus once it is set. At the same time a Cartwright coating, which greatly improved both the speed and the resolving power, was applied to the lens elements.

The finished camera which has not been changed since this time (1941) is shown in Figure 4*A*.

A paper explaining the use of this camera and its value for teaching and research was presented by Dr. E. R. Witwer[14] before the Radiological Society of North America at its San Francisco meeting, December, 1941. Later, a brief note illustrating its utilization in the study of peristaltic action of the human esophagus was published.[3]

For the actual practical employment of

this instrument, however, exposure time and total exposure of the patient to radiation is, in itself, the most serious remaining problem and various work has been done upon it. The first single factor which enters into this general problem is the factor of film exposure time. In the ordinary type of motion picture camera, the shutter is closed approximately one-half of the time; obviously, then the patient is receiving useless exposure during this period. Attempts to synchronize the output of the roentgen tube with the shutter time of the camera have been made[9] but these necessarily entail a considerable amount of technical difficulty involving the rapid switching of the high voltage primary.

It appeared to us at the very beginning that a much simpler solution was the use of a shutterless camera. With the aid of Mr. Rex B. Wilsey of the Eastman Kodak Company such a camera was constructed and, referring again to Figures 1 and 4, it will be seen that a very simple yet highly successful mechanism was evolved.

A variable speed electric motor, operating through a train of reduction gears, drives a rotating cam which in turn drives the film transport mechanism. The drive cam, having rotated the driven cam through approximately one-third of a revolution and passed its dead center, disengages and the remainder of the rotary motion of the film transport mechanism is accomplished by means of a powerful rapid spring action. Inside the camera a claw (Fig. 4), driven by a crank arm on the end of the driven cam shaft, accomplishes the actual film transport. The center of rotation of the claw mechanism is fastened by a ring bearing to a rigid post so that the claw describes a complete lunar triangle with each revolution of the shaft. The down stroke of the claw is actuated by the spring previously described and takes place in approximately one millisecond.

The significant point is that the film transport between frames is so fast that neither blurring of the image nor exposure between frames can occur, and consequently all of the useful exposure time is recorded on the film.

Naturally, there are points in favor of either type of exposure mechanism. Where slow body motions are to be studied, as, for example, ordinary peristaltic action of the stomach, a synchronized mechanism allowing for very slow speed and interval exposures to radiation is to be preferred. However, this problem is no different from

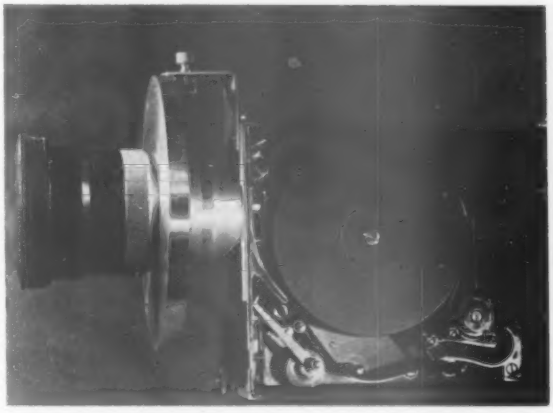

Fig. 4*A*. Finished lens assembly and focusing ring. Also shown is the fast acting claw mechanism which transports the film.

Fig. 4*B*. Motor drive mechanism shown with the cover off. The cams are shown in the position in which they are just beginning to engage. A boss is provided on the drive cam to permit mounting a microswitch for a control of roentgen-ray primary circuits at this point when synchronized operation is desired. The drum on the opposite end of the motor shaft is the speed control and provides accurate speeds continuously variable from 3 to 24 frames per second.

the standard laboratory one involving interval timing for microscopic or growth study motion pictures and can be solved with any type of camera, including this one, and a suitable electronic control mechanism for the roentgen-ray exposure. For the body motions of most immediate interest, such as normal and abnormal heart motion, hilar shadow motion, joint relationships in action, angiography, and nearly all of the ordinary problems amenable to study by this technique, the fast action continuous exposure technique still appears to be superior to any other so far developed.

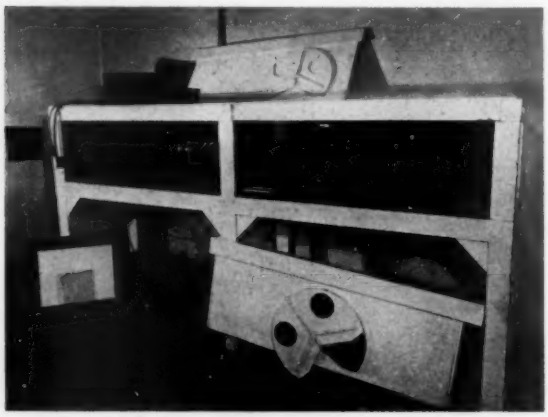

FIG. 5*A*. Complete assembly open to show details. Also shown are the roentgen-ray portal in the wall with one of the limiting diaphragms in place, the relay box through which the roentgen-ray output is controlled and the manual controls for the camera and the roentgen-ray machine which are long enough to permit control of the equipment from any place in the room. Also shown are some technical details, such as a piece of screen wire used for checking focus and alignment. The entire assembly is somewhat distorted due to the fact that this photograph had to be taken by a wide angle lens.

Having obtained a suitable camera and screen, the next immediate problem is the construction of a housing for these components. Where a single focal distance will be sufficient, as in the study of cerebral angiography, a single unit may be constructed and may be mounted together with a tube at a fixed distance, and the entire mechanism made mobile and adjustable to permit cinefluorography at various angles. Holmgren[5] has already constructed such an installation and with it produced excellent results, particularly in cerebral angiography.

For general teaching and research purposes, however, a more generalized unit is required and, if different focal distances and screen sizes are to be used, some mobility must be sacrificed.

Figure 5*A* shows the complete installation for cinefluorography at this institution. The camera housing consists of a wooden box 8 feet 6 inches in length and 18 inches by 24 inches inside dimension. Two panels of the box are removable and these are also fitted with hand holes and light-proof sleeves through which the operator may reach for technical procedures with the camera. The hand holes are closed completely by a rotating gate. In the illustration, both movable panels, which slide upward out of their channels, are shown removed from the side of the box. One shows the rotating gate open and the other closed The two light-tight sleeves are on the same horizontal plane and are behind the two lower openings of the three shown. The upper opening is fitted over with a deep red safety glass and was used originally for visual control while removing film from the camera when, in the early part of this work, film sensitive only to blue-violet light was used. With modern film the red lights are not used and film manipulations are done entirely by touch. The floor of the box is fitted with a track on which the camera mount can be moved and maintain precise centering on the fluoroscopic screen throughout the length of its travel. Along the side of this track is an index distance scale calibrated for two types of screens.

The track, the index and the locking device for holding the camera in position are shown in detail in Figure 5*B*. The end of the box nearest the tube is fitted with a light-proof slot mechanism into which the fluoroscopic screen in its frame and protected by a thick layer of lead glass can be inserted. For many purposes, a plane screen

14 by 17 inches in size, or smaller, and fitting flush into the end of the box is used.

It was soon found, however, that for studies of the head and certain other parts of the body, it was very advantageous to have a smaller screen which projected from the box far enough to permit a patient's shoulder to pass the edge of the screen with the patient either in the horizontal or the upright position. For this reason the 10 by 12 inch screen illustrated in Fig 5*C* was constructed on a mount which slips into the same light-proof slot as the ordinary plane screen. This construction has proved to be

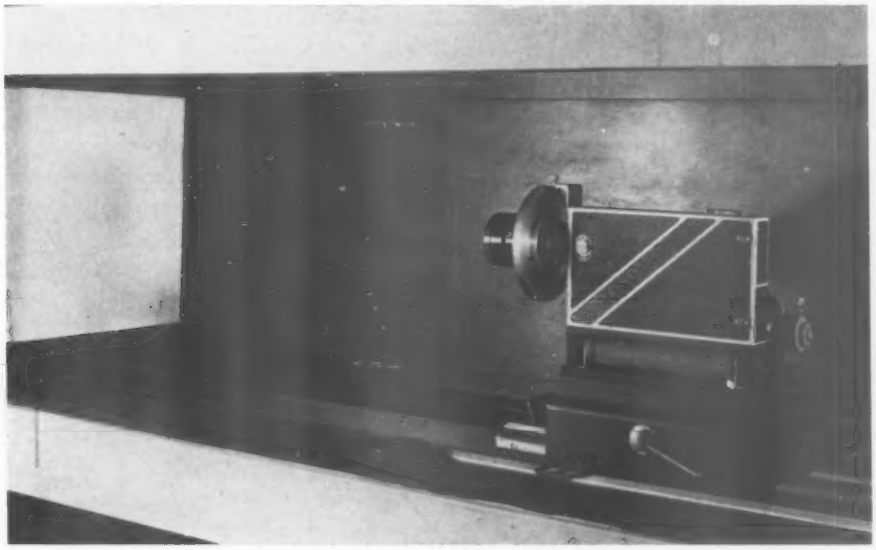

FIG. 5*B*. Detail of arrangement of the plane screen, the camera on its track, the distance index and locking mechanism.

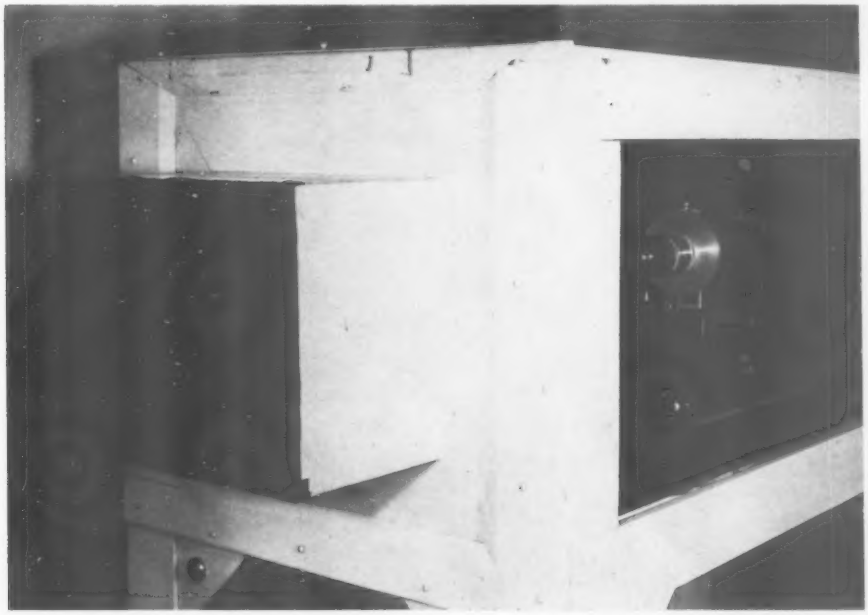

FIG. 5*C*. Detail of the small area projecting screen and relationship of the camera to the screen.

very useful. The necessity for these two arrangements of the screen requires two calibrations of the screen distance on the camera track. Distance is chosen such that the desired part of the screen exactly fills the space of the frame on the film and the lens setting is then corrected for this distance. Once these calibrations have been made, the actual setup and subsequent changes can be made in a matter of seconds.

The advantage of such a versatile arrangement may be illustrated by considering a case in which, first the entire chest is to be seen and then, after the significant points have been shown in their general relationship to each other, it is desired to "frame down" upon some specific area of interest, such as an aortic aneurysm or other relatively small object, and bring this out at full screen size in complete detail.

Originally, both the height of the tube and the height of the camera from the floor could be varied but this was found to be unnecessary and undesirable in that exact alignment was hard to maintain. In the present arrangement they are at a permanently fixed distance of 41 inches from floor to center line of beam. This height from the plane of the floor was chosen to permit the use of a stretcher or a small mobile table in front of the camera. For ordinary purposes, ambulatory patients are seated on a stool, the height of which can be varied to suit the physical dimensions of the patient. Non-ambulatory cases and procedures such as heart catheterization, which require the patient to be in a horizontal position, are carried out with equal facility. The room and all its necessary appointments are so arranged that a sterile field can be set up in front of and at both sides of the camera tunnel near the front, and any surgical procedure which is likely to be required can be conducted safely. It must be admitted that in the present installation the room is too small and the space at the screen end of the camera tunnel much too crowded for comfort. However, it meets all necessary requirements.

The last major problem in cinefluorography is the roentgen tube itself and its attendant power plant. This, of course, is a very large item of expense and must meet certain specific requirements in order to be satisfactory. In the first place, a tube having a reasonably small focal spot and, at the same time, capable of carrying high power input for relatively long periods of time is required. There is no advantage in an extremely small focal spot, since the resolution of the screen is the limiting factor, and for all practical purposes a Type C (3.2^2 mm.) is the smallest required. In the installation shown, the tube is water-cooled and is mounted in a lead box at a fixed position in such a manner that its beam emerges through the portal in the wall shown in front of the camera housing. A relatively long target screen distance is used in order to reduce the exposure to the patient and to reduce distortion as much as possible. It is always a strong temptation to reduce the target screen distance and thereby gain intensity. However, the exposure to the side of the patient distant from the screen and near the focal spot increases so rapidly that the allowable exposure time and, hence, the amount of actual study value that may be gained from the film is seriously reduced by this procedure.

There are two other technical difficulties which can be grouped together in that they are quite beyond the aid of those actually interested in cinefluorography and are rather in the hands of the manufacturing companies, who have made great strides in their perfection within the last few years. They are (1) the problem of a fast screen with high resolution and low lag, and (2) the problem of fast film with fine grain. These have both been solved to the point where they are no longer major items of concern.

There is little reference in the literature as to the actual exposure required by the screen or sustained by the patient, although Stewart[11] does give his factors and shows that, with 100 kv., 125 ma. for 40 cm. target skin distance, the tolerance limit would be approximately forty-eight seconds, and

his exposure time was five seconds, or roughly 10 per cent of this amount. We have found fifteen second exposures to be much more satisfactory and have also, found it necessary to obtain approximately 0.2 r per second on the surface of the screen in order to take satisfactory films at the rate of 12 frames per second.*

Two minor technical details which should be mentioned are (1) the use of a celluloid filter, which has one advantage over aluminum in that the light from the filament of the tube can be seen to warn the team working with the camera that the tube is ready to be activated, and (2) the use of a lead glass on the screen which does reduce its efficiency but has been proved absolutely essential for protection purposes, if any extensive amount of work is to be done. These two compromises with necessity are therefore tolerated.

The roentgen-ray requirements are met in this installation by a tube operating at 115 kv. and 50 ma. at a distance of 90 cm. and using a 3 mm. celluloid filter. This installation was found to deliver 1.6 per r second to the patient's back, and hence a fifteen second exposure over a reasonably restricted area is not considered excessive. Lead diaphragms are used to limit the beam to the area being studied.

The obvious answer to the exposure problem is the use of an electron multiplier screen. However, the development of such a screen has been retarded by the high costs involved, although it has been discussed for many years.

The value of the cinefluorographic technique as a teaching method is probably best exemplified by the teaching film itself and is not readily amendable to reproduction on paper. One film produced by the apparatus illustrated here was in use through 1945 for teaching the mechanism of deglutition and the peristaltic action of the esophagus.

Figure 6 shows the technique for studying the chambers of the heart by means of injected contrast medium. The subject in this case is a dog and even the brief portions of film shown here illustrate the rapidity, and at the same time the clarity,

Fig. 6. Left to right lateral oblique projection. Contrast medium in heart and aorta of a dog. Note particularly shape of chambers and filling of subclavian artery.

* Various speeds must be used but for many purposes 12 frames per second is satisfactory in itself and may also be double printed to give standard commercial speed of 24 frames per second for teaching films.

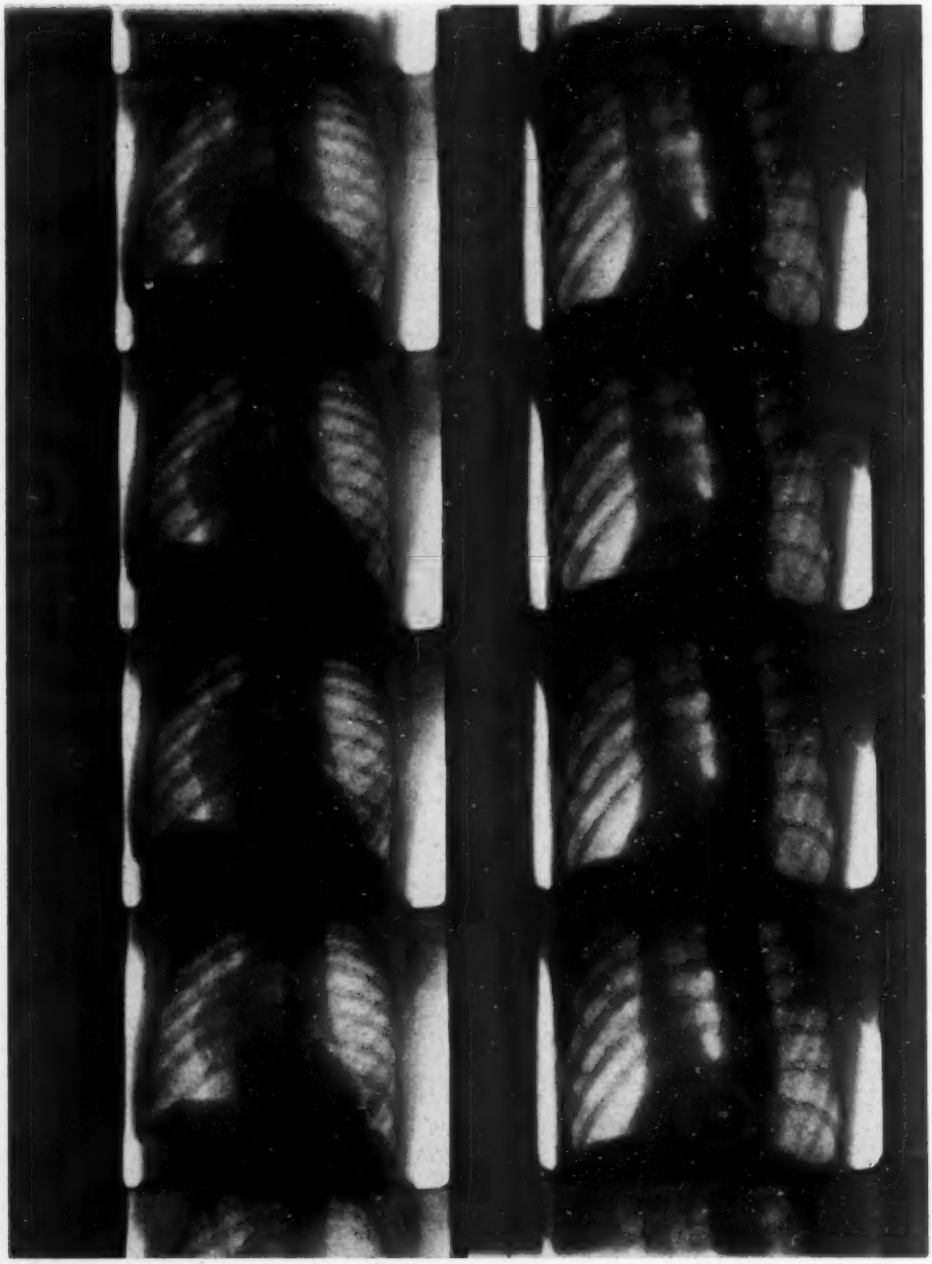

FIG. 7. Posteroanterior and lateral projection of heart with aneurysm of ascending aorta.

with which the chambers and the associated great vessels fill and empty.

Figure 7 is an posteroanterior and lateral view of a young person with an aneurysm of the ascending aorta. While the usual roentgen studies of the chest may leave considerable doubt as to the meaning of a shadow of this sort, it is easily shown on moving picture film and easily identified. The film is then useful for teaching purposes and in a short period of time a large number of cases illustrating unusual lesions can be gathered for the benefit of future classes.

Figure 8 shows the application of the cinefluorographic technique to an actual

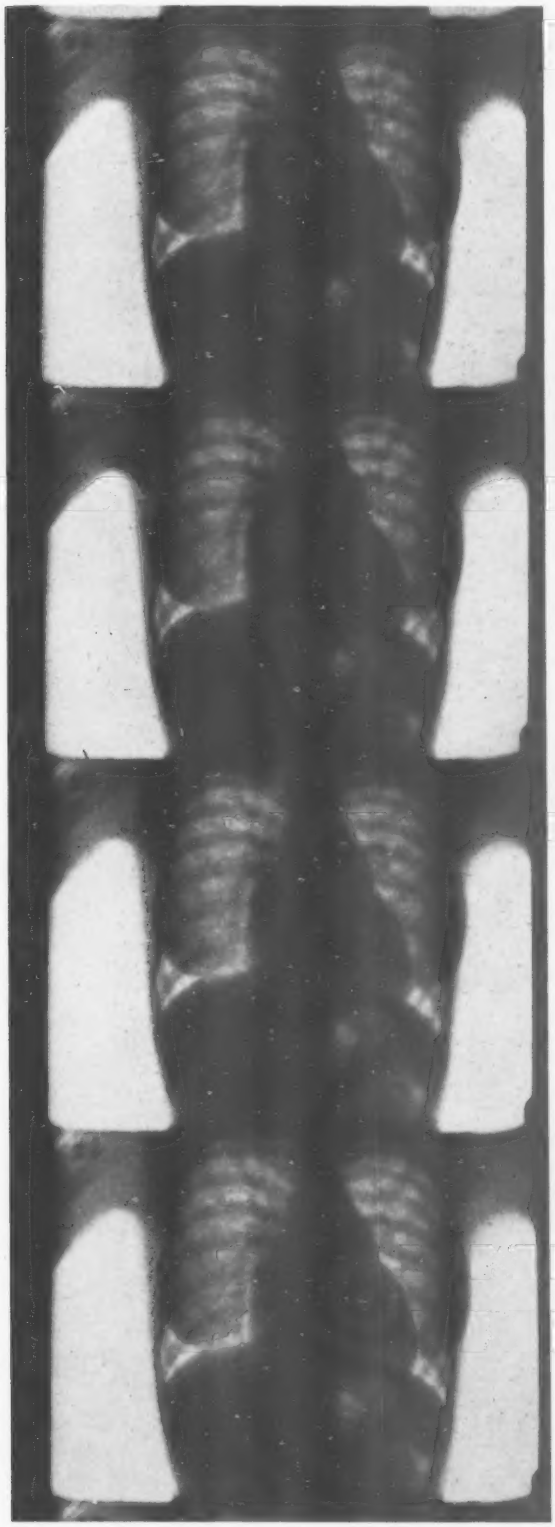

Fig. 8. Patent ductus arteriosus. Child aged eleven years, later treated successfully by surgery.

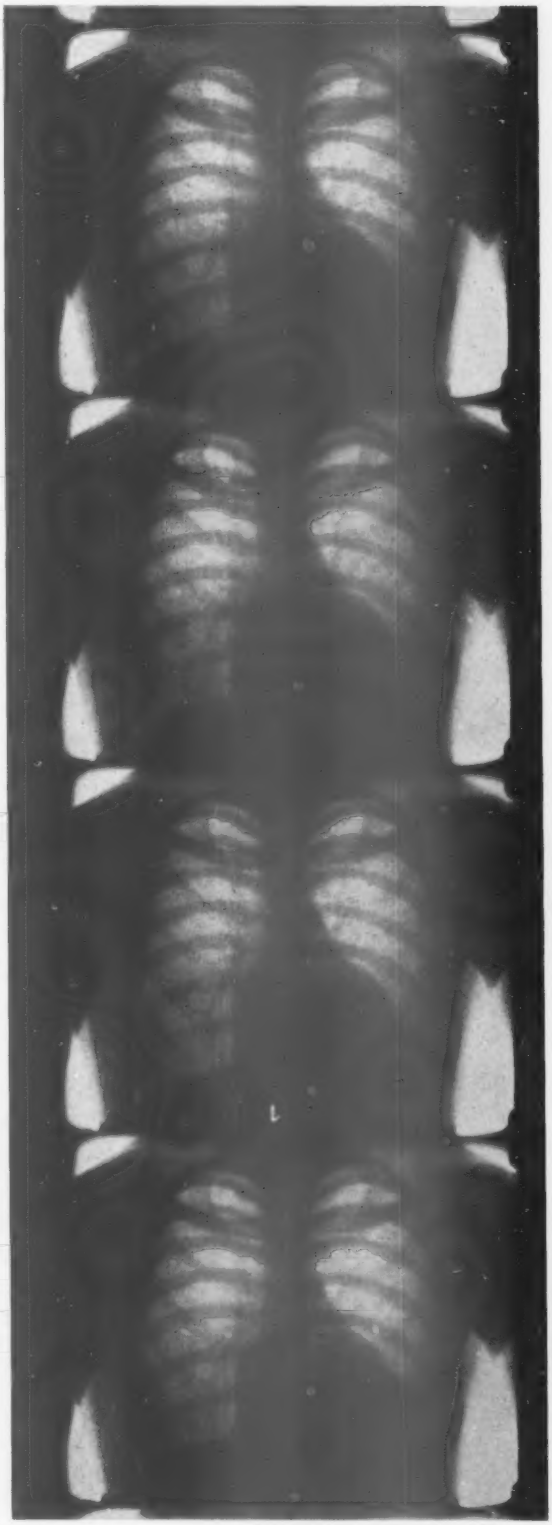

Fig. 9. Mitral stenosis. Original film shows characteristic motion and distortion, which is seen to a limited degree in the print.

diagnostic problem, in this case a girl, aged eleven years, with a patent ductus arteriosus.

Figure 9 illustrates the characteristic malformation associated with mitral stenosis and makes it possible to show an entire class exactly what they may expect to see in the roentgenoscope.

All of these films and many others like them, illustrating different conditions, are of great value in teaching medical students, since they make clear the underlying cause of what the student sees and what he hears in his stethoscope.

SUMMARY AND CONCLUSIONS

1. The cinefluorographic technique with modern equipment is an entirely practical procedure.

2. It is directly applicable to the study of unusual cases and aids diagnosis by making a permanent record of the motion and aberrations of rapidly moving objects, such as the heart, or contrast medium in the great vessels, including cerebral angiograms.

3. It is a primary technique for research and gives a permanent record of comparison studies on the effect of medication such as digitalis, or the normal or anomalous paths taken in contrast studies.

4. It is an ideal teaching method in that typical cases of all kinds may be shown to entire classes of students and the presentation of the film may be continued as long or repeated as often as may be necessary.

5. Modern cinefluorography does not require excessive exposure to the patient and is entirely safe for the operators.

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REFERENCES

1. BARCLAY, A. E., FRANKLIN, K. J., and PRICHARD, M. M. L. X-ray cinematography in research. *Brit. J. Radiol.*, 1940, *13*, 227–234.
2. COLE, L. G. Roentgenocinematography of stomach and cap. AM. J. ROENTGENOL., 1914, *1*, 212–216.
3. CORRIGAN, K. E., and HAYDEN, H. S. Mechanism of deglutition. AM. J. ROENTGENOL. & RAD. THERAPY, 1944, *52*, 559–560.
4. DE CASTRO, J. M. Fundamental principles in application of cineroentgenography as auxiliary method to roentgen diagnosis. AM. J. ROENTGENOL. & RAD. THERAPY, 1947, *57*, 103–114.
5. HOLMGREN, B. S. Roentgen cinematography as routine method. *Acta radiol.*, 1945, *26*, 286–292.
6. JANKER, R. Roentgen cinematography. AM. J. ROENTGENOL. & RAD. THERAPY, 1936, *36*, 384–390.
7. JARRE, H. A. Roentgen cinematography. In: Medical Physics. Otto Glasser, Editor. Year Book Publishers, Inc., Chicago, 1944, pp. 1259–1260.
8. MACINTYRE, J. X-ray records for cinematograph. *Arch. Skiag.*, 1897, *1*, 37.
9. REYNOLDS, R. J. Some experiments on production of rapid serial roentgenograms from screen image by means of cinematographic camera. AM. J. ROENTGENOL. & RAD. THERAPY, 1928, *19*, 469–473.
10. REYNOLDS, R. J. Cineradiography. AM. J. ROENTGENOL. & RAD. THERAPY, 1935, *33*, 522–528.
11. STEWART, W. H., HOFFMAN, W. J., and GHISELIN, F. H. Cinefluorography. AM. J. ROENTGENOL. & RAD. THERAPY, 1937, *38*, 465–469.
12. STEWART, W. H., and GHISELIN, F. H. Paradoxical movement of diaphragm and mediastinal shift; cinefluorographic studies. AM. J. ROENTGENOL. & RAD. THERAPY, 1939, *41*, 926–930.
13. STEWART, W. H., BREIMER, C. W., and MAIER, H. C. Cineroentgenographic diagnosis of congenital and acquired heart disease. AM. J. ROENTGENOL. & RAD. THERAPY, 1941, *46*, 636–640.
14. WITWER, E. R. Roentgen investigation of esophagus. Refresher Course, Annual Meeting of the Radiological Society of North America, San Francisco, 1941. *Radiology*, 1941, *37*, 368.

DEPARTMENT OF TECHNIQUE

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MODIFIED SPOT SCANOGRAPHY

By J. SHERIDAN BELL, M.D.,* *and* WALTER A. L. THOMPSON, M.D.†
NEW YORK, NEW YORK

A MODIFIED method of spot scanography that is in use at the New York Orthopaedic Dispensary and Hospital for measurement of bone length is herewith described.

A steel rule $\frac{1}{64}$ inch thick and 36 inches long and graduated in consecutive inches by depressed numbers and markings is placed on the centerline of the roentgen table. On each side of the rule is placed a strip of galvanized iron $\frac{1}{64}$ inch thick, 3 inches wide, and 36 inches long. These strips are necessary for uniform filtration of the roentgen rays. The rule and strips are fastened to the table with tape.

For the six exposures necessary to measure the lower extremities an 11 by 14 inch film is used. The cassette is covered with a sheet of lead having two holes 4 inches in diameter, one being closed with a circular piece of lead while an exposure is being made through the other. From the end of the table the roentgen tube is centered to the midline before the patient is positioned. The part to be exposed and the open hole in the lead are centered to the tube.

From the roentgenograms obtained the distance between any two points at opposite bone ends can be readily calculated. Either edge of the rule may be selected as the base of a right triangle. If both points are on the same side of the edge, the difference in the distances of the points from the edge becomes the altitude of the triangle whose hypotenuse is the distance between the points; if the points are on opposite sides of the edge, the sum of the distances from the edge is the altitude. However, for practical purposes in the measurement of long bones such as the femur and tibia no

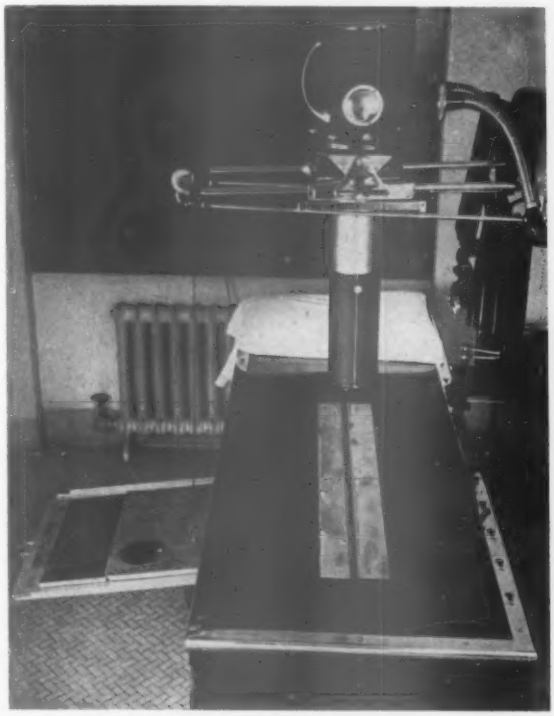

Fig. 1.

* Radiologist, New York Orthopaedic Dispensary and Hospital.
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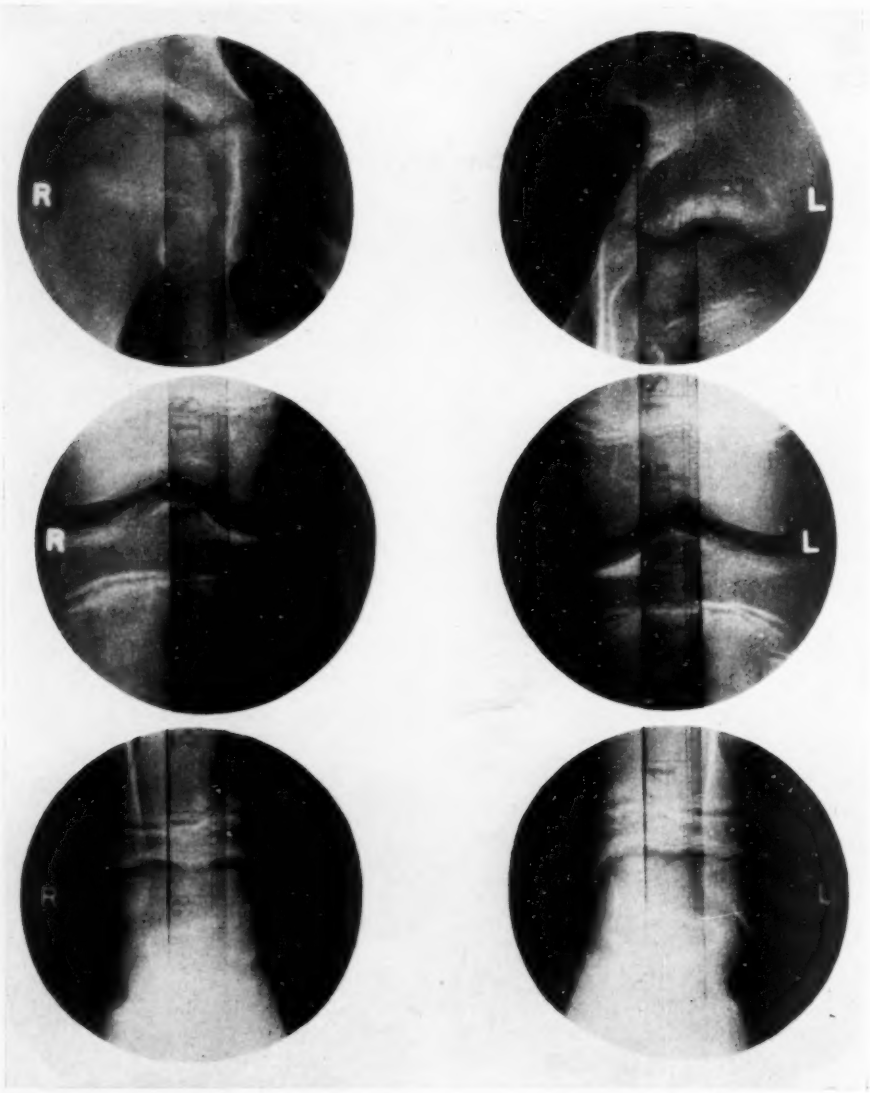

FIG. 2.

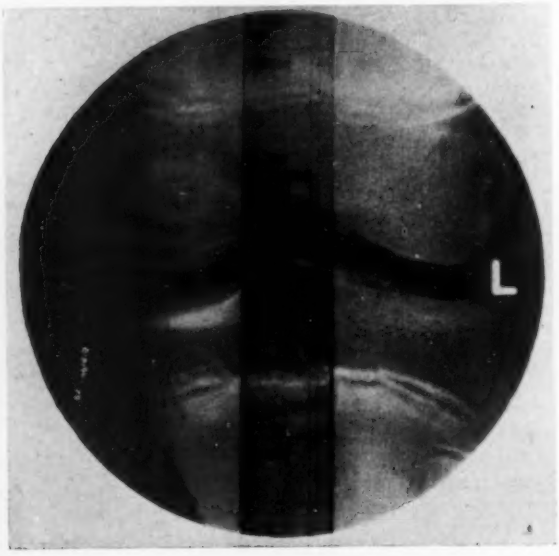

FIG. 3.

calculation to obtain the hypotenuse is necessary as the error is very small, subtracting the low reading from the high reading being all that is necessary.

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Vol. 63, No. 6

THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY

Editor: Lawrence Reynolds, M.D. *Assistant Editor:* Ruth Bigelow, B.S.

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Consulting Editorial Board: See front cover.

Published by: Charles C Thomas, Publisher, 301–327 East Lawrence Avenue, Springfield, Illinois.

Issued monthly. Annual subscription: United States, Mexico, Cuba, Central and South America, $10.00; Canada, $11.00; other countries, $12.00. Advertising rates submitted on application. Editorial office, 110 Professional Building, Detroit 1, Michigan. Office of publication, 301–327 East Lawrence Avenue, Springfield, Illinois. Information of interest to authors and readers will be found on page iv.

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EDITORIALS

EMPHYSEMA, SILICOSIS, AND COAL MINERS

THE correlation of roentgenologic chest findings and clinical symptoms in anthracosilicosis is frequently poor, especially in the earlier manifestations of the disease. For this reason a determination of pulmonary function is of great value in evaluating the degree of pulmonary insufficiency present.

Emphysema accounts for only a part of the impairment. There are many instances where clinical symptoms are great, yet the degree of emphysema is not significant. The recent studies of Motley, Lang and Gordon[1,2] in one hundred anthracite coal miners, all of whom had respiratory complaints, demonstrate clearly the importance of correlating pulmonary function with clinical and roentgenologic findings before the actual disability can be determined.

In the first study reported by these authors the degree of emphysema was expressed by determining the residual air as a per cent of the total lung volume. On the basis of these determinations five groups were arbitrarily set up:

(1) No emphysema, in which the per cent of residual air as compared to lung volume was 25 per cent or less,
(2) Slight degree of emphysema, in which the per cent of residual air was 25 per cent to 35 per cent,
(3) Moderate degree of emphysema (35 per cent to 45 per cent),
(4) Advanced degree of emphysema (45 per cent to 55 per cent), and
(5) Far advanced degree of emphysema (65 per cent or more).

[1] Motley, H. L., Lang, L. P., and Gordon, B. Pulmonary emphysema and ventilation measurements in one hundred anthracite coal miners with respiratory complaints. *Am. Rev. Tuberc.*, 1949, *59*, 270–288.

[2] Motley, H. L., Lang, L. P., and Gordon, B. Studies on the respiratory gas exchange in one hundred anthracite coal miners with pulmonary complaints. *Am. Rev. Tuberc.*, 1950, *61*, 201–225.

On the basis of this logical classification it was shown that there was a lack of correlation between the roentgenographic findings as far as silicosis was concerned and the degree of emphysema. For example, in sixty-seven patients who had the third stage of silicosis (classification of Pancoast and Pendergrass) there were eight patients in whom there was no emphysema and fifteen in whom the degree of emphysema was only slight. In most cases with far advanced emphysema and third stage silicosis, the chest roentgenograms were satisfactory for predicting the degree of emphysema.

Because of this poor correlation, it is necessary to have physiological data which will permit an evaluation of pulmonary function with respect to the transporting of oxygen into and the removal of carbon dioxide from the blood of these individuals at rest and after exercise. The data necessary for such evaluation are:

(1) Ventilation measurements (maximal breathing capacity and vital capacity),
(2) Degree of pulmonary emphysema as determined by the residual air expressed as per cent of total lung volume,
(3) The extent of the distribution impairment due to unequal alveolar aeration and perfusion with a consequent decrease in arterial pO_2 and per cent saturation, and
(4) Measurement of ventilation efficiency (oxygen uptake from and carbon dioxide addition to the air breathed).

Each of these factors may account singly or in combination with other factors for the impairment of oxygen transport.

Pulmonary emphysema accounts for only

part of the impairment of pulmonary function in anthracosilicosis. In a considerable number of cases with pulmonary insufficiency the degree of emphysema was not significant. The fibrosis present in some cases of anthracosilicosis may or may not produce significant emphysema, but it can interfere with the uniform aeration of the alveoli when alveoli are poorly ventilated. There results an increase of the mean pressure gradient of partial oxygen tension (pO_2) between the alveoli and arterial blood. Distribution, one of the factors contributing to the alveolar-arterial pO_2 gradient, may be defined as variations in the different parts of the lung, or the ratio of alveolar ventilation to alveolar perfusion. Fibrosis also obliterates the blood supply to alveoli, so that the alveoli may be ventilated but not function in gaseous exchange. Thus, the physiological dead space is increased and the efficiency of the O_2 oxygen removal is reduced. It is well known, for example, that following collapse of one lung pulmonary efficiency improves because of the removal of dead space which existed in the removed lung.

The impairment of distribution of air in the lungs may produce marked arterial oxygen unsaturation, even in the absence of emphysema and with a normal maximal breathing capacity. An accurate clinical evaluation of disability in such a patient is unlikely when the roentgenographic findings are minimal. The per cent of oxygen uptake and the carbon dioxide addition to the air breathed is helpful in the overall evaluation of the impairment present, but this test has slight value as a single measurement. Studies on pulmonary circulation during exercise reveal definite abnormalities in chronic pulmonary disease, including a rise in pulmonary arterial pressure, and an increase in pulmonary vascular resistance as compared to the unchanged or lower arterial pressure during exercise in normal subjects.

An accurate evaluation of the degree of pulmonary functional impairment requires measurement of ventilation, residual air, oxygen uptake from the air breathed, and arterial blood studies during both rest and exercise. In selected cases measurements on the pulmonary circulation may be necessary. Because wide individual variations in these determinations do occur, the use of any single test is unsatisfactory for the appraisal of the disability present.

The articles and methods of Motley and his colleagues have medicolegal significance since some labor boards have considered emphysema *per se* a compensable disease, whether it be associated with silicosis or not. This is quite ridiculous since all physicians know that emphysema frequently occurs in the absence of silicosis on the basis of several etiological factors among which are chronic asthma and chronic bronchitis.

Gray[3] has pointed out that confusion exists regarding the meaning of the term emphysema. It is generally used in the morphologic sense, referring either to the form of the chest (clinical) or to the confluence of the alveoli (pathological). If the term is related to residual volume, it has a geometric rather than a functional connotation. However, the real pathological physiology consists of impaired ventilation capacity, chiefly from obstruction, and impaired alveolar-arterial gas exchange, neither of which is due solely to the form of the chest, confluence of alveoli, or to increased residual volume. It is best for emphysema to remain a morphological word; so, some terms are needed to describe the pathological physiology.

A. C. Ivy, Ph.D., M.D., D.Sc.

[3] Gray, J. S., Professor of Physiology, Northwestern University. Personal communication.

DORWIN LEWIS PALMER
1888–1948

Dorwin Lewis Palmer, after a lingering illness, died in Santa Barbara, California, on December 27, 1948. Dr. Palmer was born October 5, 1888, in Carlisle, Ohio. He was graduated from the University of Oregon Medical School in 1915, and served his

Dorwin Lewis Palmer

internship at the Multnomah County Hospital from 1914 to 1916. He was a veteran of World War I, having served in France as Captain at Base Hospital No. 46. He was active in medical affairs in Portland, Oregon, until his retirement in 1945, heading the Department of Radiology at the Portland Clinic from its inception in 1921. He served as associate clinical professor and head of the division of radiology at the University of Oregon Medical School. Dr. Palmer was certified by the American Board of Radiology in 1934, and was a member of the American Medical Association and the American Roentgen Ray Society. He served on the local Selective Service Board during World War II. He is survived by his wife, Mrs. Theresa Palmer, and one son.

Dr. Palmer had the rare quality of true friendliness and kindness. Throughout the years of his illness and disability, grateful patients at the Portland Clinic continued to ask regarding his welfare. Both he and my father took up radiology during the first World War and began a friendship which—happily for me—I was the beneficiary of for many years. His approach to radiology was of a practical nature, and his humor and common sense made the study of radiology under him a pleasure and a treat. His ill health became manifest in 1941 and he was gradually forced to give up his activity until a stroke in 1945 made complete retirement necessary. Throughout his illness, his keen interest in radiology continued, and one of my last contacts with him was during a postgraduate course in radiology in 1942 in Minneapolis which he attended despite the knowledge of his limitations due to his disability. Always having been an active "little dynamo," he was unable to adjust himself and became obsessed with the idea that he was a burden to his family and friends. To those of us who knew him well, he could never have been a burden to anyone, and his passing creates a void that cannot be filled.

MELVIN ASPRAY, M.D.

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

MEETINGS OF ROENTGEN SOCIETIES*

United States of America

American Roentgen Ray Society
Secretary, Dr. Barton R. Young, Germantown Hospital, Philadelphia 44, Pa. Annual meeting: Jefferson Hotel, St. Louis, Mo., Sept. 26–29, 1950.

American Radium Society
Secretary, Dr. H. F. Hare, 605 Commonwealth Ave., Boston, Mass. Annual meeting: Roosevelt Hotel, New York, N. Y., May 25–26, 1950.

Radiological Society of North America
Secretary, Dr. D. S. Childs, 607 Medical Arts Bldg., Syracuse, N.Y. Annual meeting: Palmer House, Chicago, Ill., Dec. 10–15, 1950.

American College of Radiology
Executive Secretary, William C. Stronach, 20 N. Wacker Drive, Chicago 6. Annual meeting: San Francisco, Calif., June 25, 1950.

Section on Radiology, American Medical Association
Secretary, Dr. Paul C. Hodges, 950 E. 59th St., Chicago, Ill. Annual Meeting: San Francisco, Calif., June 26–30, 1950.

Alabama Radiological Society
Secretary, Dr. W. W. Anderson, Tuscaloosa, Ala. Meets time and place Alabama State Medical Association.

Arizona Association of Pathologists and Radiologists
Secretary, Dr. R. Lee Foster, 507 Professional Bldg., Phoenix, Ariz. Two regular meetings a year. The annual meeting at time and place of State Medical Association and interim meeting six months later.

Arkansas Radiological Society
Secretary, Dr. Fred Hames, 511 National Bldg., Pine Bluff, Ark. Meets every three months and also at time and place of State Medical Association.

Atlanta Radiological Society
Secretary, D. W. W. Bryan, 490 Peachtree St., N.E., Atlanta, Ga. Meets monthly, except during three summer months, on second Friday evening.

Brooklyn Roentgen Ray Society
Secretary, Dr. J. J. Daversa, 345 75th St., Brooklyn, N. Y. Meets monthly fourth Tuesday, Oct. through April.

Buffalo Radiological Society
Secretary, Dr. Mario C. Gian, 610 Niagara St., Buffalo, N. Y. Meets second Monday evening each month, October to May inclusive.

Central New York Roentgen Ray Society
Secretary, Dr. Dwight V. Needham, 608 E. Genesee St., Syracuse N. Y. Meets January, May, November.

Central Ohio Radiological Society
Secretary, Dr. Paul D. Meyer, Grant Hospital, Columbus, Ohio. Meets at 6:30 P.M. on second Thursday of October, December, February, April, and June at Seneca Hotel, Columbus, Ohio.

Chicago Roentgen Society
Secretary, Dr. John H. Gilmore, 720 N. Michigan Ave., Chicago 11, Ill. Meets second Thursday of each month October to April inclusive at the University Club.

Cincinnati Radiological Society
Secretary, Dr. E. C. Elsey, 927 Carew Tower, Cincinnati 2, Ohio. Meets last Monday of each month, September to May, inclusive.

Cleveland Radiological Society
Secretary, Dr. J. R. Hannan, Cleveland Clinic, Cleveland 6, Ohio. Meetings at 6:30 P.M. on fourth Monday of each month from October to April.

Colorado Radiological Society
Secretary, Dr. Paul E. RePass, 306 Republic Bldg., Denver 2, Colo. Meets third Friday of each month at University of Colorado Medical Center or at Denver Athletic Club.

Connecticut Valley Radiologic Society
Secretary, Dr. E. W. Godfrey, 1676 Boulevard, West Hartford, Conn. Meets second Friday Oct. and April.

Dallas-Fort Worth Roentgen Study Club
Secretary, Dr. X. R. Hyde, Medical Arts Bldg., Fort Worth, Texas. Meets in Dallas on odd months and in Fort Worth on even months, on third Monday, 7:30 P.M.

Detroit Roentgen Ray and Radium Society
Secretary, Dr. W. G. Belanger, Harper Hospital. Meets monthly on first Thursday from October to May, at Wayne County Medical Society Building.

East Bay Roentgen Society
Secretary, Dr. Dan Tucker, 434-30th St., Oakland 9, Calif. Meets first Thursday each month at Peralta Hospital, Oakland.

Florida Radiological Society
Secretary, Dr. F. K. Hurt, Riverside Hospital, Jacksonville, Fla. Meets twice annually, in the spring with the annual State Society meeting, and in the fall.

Georgia Radiological Society
Secretary, Dr. R. C. Pendergrass, Americus, Ga. Meets in mid-winter and at annual meeting of Medical Association of Georgia in the spring.

Greater Miami Radiological Society
Secretary, Dr. David Kirsh, 712 duPont Bldg., Miami 32, Florida. Meets last Wednesday of each month at 8:00 P.M. at Veterans Administration Regional Office.

Houston X-ray Club
Secretary, Dr. Curtis H. Burge, 3020 San Jacinto St. Houston 4, Texas. Meets fourth Monday each month.

Radiological Society of Kansas City
Secretary, Dr. Arthur B. Smith, 800 Argyle Bldg., Kansas City, Mo. Meets third Thursday of each month.

Illinois Radiological Society
Secretary, Dr. Wm. DeHollander, St. John's Hospital, Springfield, Ill. Meets three times a year.

Indiana Roentgen Society
Secretary, Dr. William M. Loehr, 712 Hume-Mansur Bldg., Indianapolis 4. Meets second Sunday in May.

Iowa X-Ray Club
Secretary, Dr. Arthur W. Erskine, 326 Higley Bldg., Cedar Rapids, Iowa. Luncheon and business meeting during annual session of Iowa State Medical Society. Special meetings by announcement.

Kansas Radiological Society
Secretary, Dr. Anthony F. Rossitto, Wichita Hospital, Wichita, Kan. Meets annually with State Medical Society.

Kentucky Radiological Society
Secretary, Dr. W. C. Martin, 321 W. Broadway, Louisville. Meets annually in Louisville on first Saturday in Apr.

Kings County Radiological Society
Secretary, Dr. Marcus Wiener, 1430-48th St., Brooklyn, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:45 P.M.

Los Angeles Radiological Society
Secretary, Dr. Wybren Hiemstra, 1414 S. Hope St., Los Angeles 15, Calif. Meets second Wednesday each month at Los Angeles County Medical Assn. Building.

Louisiana Radiological Society
Secretary, Dr. J. R. Anderson, 1130 Louisiana Ave., Shreveport. Meets annually during Louisiana State Medical Society Meeting.

* Secretaries of societies are requested to send timely information promptly to the Editor.

LOUISVILLE RADIOLOGICAL SOCIETY
Secretary, Dr. E. L. Pirkey, Louisville General Hospital, Louisville 2, Ky. Meets monthly on second Friday at Seelbach Hotel, Louisville.

MIAMI VALLEY RADIOLOGICAL SOCIETY
Secretary, Dr. G. A. Nicoll, 134 Apple St., Dayton, Ohio. Meets second Friday of fall and winter months.

MICHIGAN ASSOCIATION OF ROENTGENOLOGISTS
Secretary, Dr. R. D. McDuff, 220 Genesee Bank Bldg., Flint 3, Mich.

MILWAUKEE ROENTGEN RAY SOCIETY
Secretary, Dr. T. J. Pfeffer, 839 N. Marshall St., Milwaukee 2, Wis. Meets monthly on second Monday at University Club.

MINNESOTA RADIOLOGICAL SOCIETY
Secretary, Dr. L. A. Nash, 572 Lowry Medical Arts Bldg., St. Paul 2, Minn. Meets three times annually, once at time of State Med. Assn., and in spring and fall.

NEBRASKA RADIOLOGICAL SOCIETY
Secretary, Dr. J. E. Downing, 816 Medical Arts Bldg., Omaha, Nebr. Meets fourth Thursday of each month at 6 P.M. at Omaha or Lincoln.

NEW ENGLAND ROENTGEN RAY SOCIETY
Secretary, Dr. George Levene, Massachusetts Memorial Hospitals, Boston, Mass. Meets monthly on third Friday, Harvard Club.

NEW HAMPSHIRE ROENTGEN RAY SOCIETY
Secretary, Dr. A. C. Johnston, Elliott Community Hospital, Keene, N. H. Meets four to six times yearly.

NEW YORK ROENTGEN SOCIETY
Secretary, Dr. F. H. Ghiselin, 111 East 76th St., New York 21, N. Y. Meets monthly on third Monday, New York Academy of Medicine, at 8:30 P.M.

NORTH CAROLINA RADIOLOGICAL SOCIETY
Secretary, Dr. J. E. Hemphill, 1420 E. Fifth St., Charlotte 4, N. C. Meets in May and October.

NORTH DAKOTA RADIOLOGICAL SOCIETY
Secretary, Dr. C. O. Heilman, 807 Broadway, Fargo. Meetings by announcement. Annual session with State Medical Society in May, 1950, at Grand Forks, N.D.

NORTHERN CALIFORNIA RADIOLOGICAL CLUB
Secretary, Dr. R. L. Ayers, 726 4th St., Marysville, Calif. Meets at dinner last Monday, every second month, except June, July and August.

OHIO STATE RADIOLOGICAL SOCIETY
Secretary, Dr. E. C. Elsey, 927 Carew Tower, Cincinnati 2, Ohio.

OKLAHOMA STATE RADIOLOGICAL SOCIETY
Secretary, Dr. W. E. Brown, Tulsa, Okla. Three regular meetings annually.

OREGON RADIOLOGICAL SOCIETY
Secretary, Dr. Selma Hyman, Univ. of Oregon Medical School, Portland, Oregon. Meets monthly 2nd Wednesday, 8:00 P.M.

ORLEANS PARISH RADIOLOGICAL SOCIETY
Secretary, Dr. Joseph V. Schlosser, Charity Hospital, New Orleans 13, La. Meets first Tuesday of each month.

PACIFIC NORTHWEST RADIOLOGICAL SOCIETY
Secretary, Dr. S. J. Hawley, 1320 Madison St., Seattle 4, Wash. Meets annually in May.

PACIFIC ROENTGEN SOCIETY
Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

PENNSYLVANIA RADIOLOGICAL SOCIETY
Secretary, Dr. J. M. Converse, 416 Pine St., Williamsport. Annual Meeting: Penn Harris Hotel, Harrisburg, Pa., May 12–13, 1950.

PHILADELPHIA ROENTGEN RAY SOCIETY
Secretary, Dr. G. P. Keefer, 1930 Chestnut St. Meets first Thursday each month October to May, at 8:00 P.M., in Thomson Hall, College of Physicians.

PITTSBURGH ROENTGEN SOCIETY
Secretary Dr. E. J. Euphrat, 3500 Fifth Ave., Pittsburgh 13, Pa. Meets 6:30 P.M. at Webster Hall Hotel on second Wednesday each month, October to May inclusive.

QUEENS ROENTGEN RAY SOCIETY
Secretary, Dr. J. E. Goldstein, 88-29 163rd St., Jamaica 3, N. Y. Meets fourth Monday of each month except during the summer.

RADIOLOGICAL SECTION, BALTIMORE MEDICAL SOCIETY
Secretary, Dr. Harry A. Miller, 2452 Eutaw Place, Baltimore. Meets third Tuesday each month, Sept. to May.

RADIOLOGICAL SECTION, CONNECTICUT MEDICAL SOCIETY
Secretary, Dr. Fred Zaff, 135 Whitney Ave., New Haven, Conn. Meets bimonthly on second Wednesday.

RADIOLOGICAL SECTION, DISTRICT OF COLUMBIA MEDICAL SOCIETY
Secretary, Dr. K. C. Corley, 1835 Eye St., N. W., Washington, D. C. Meets Medical Society Auditorium, third Thursday, Jan., March, May, Oct. at 8:00 P.M.

RADIOLOGICAL SECTION, SOUTHERN MEDICAL ASSOCIATION
Secretary, Dr. Roy G. Giles, Temple, Texas.

RADIOLOGICAL SOCIETY OF NEW JERSEY
Secretary, Dr. Benjamin Copleman, 280 Hobart St., Perth Amboy, N. J. Meets annually at Atlantic City at time of State Medical Society and mid-winter at Elizabeth, N. J.

ROCHESTER ROENTGEN RAY SOCIETY, ROCHESTER, N. Y.
Secretary, Dr. A. V. Winchell, 40 Meigs St., Rochester, N. Y. Meets monthly on last Monday from September through May, 8 P.M. at Strong Memorial Hospital.

ROCKY MOUNTAIN RADIOLOGICAL SOCIETY
Secretary, Dr. Maurice D. Frazer, 1037 Stuart Bldg., Lincoln, Nebr.

ST. LOUIS SOCIETY OF RADIOLOGISTS
Secretary, Dr. H. R. Senturia, Pasteur Medical Building, St. Louis, Mo. Meets fourth Wednesday each month, except June, July, August, and September.

SAN DIEGO ROENTGEN SOCIETY
Secretary, Dr. R. F. Niehaus, 1831 Fourth Ave., San Diego, Calif. Meets monthly, first Wednesday at dinner.

SECTION ON RADIOLOGY, CALIFORNIA MEDICAL ASSOCIATION
Secretary, Dr. D. R. MacColl, 2007 Wilshire Blvd., Los Angeles 5, Calif.

SECTION ON RADIOLOGY, ILLINOIS STATE MEDICAL SOCIETY
Secretary, Dr. Harold L. Shinall, St. Joseph's Hospital, Bloomington, Ill.

SHREVEPORT RADIOLOGICAL CLUB
Secretary, Dr. R. W. Cooper, Charity Hospital, Shreveport, La. Meets monthly on third Wednesday, at 7:30 P.M., September to May inclusive.

SOUTH CAROLINA X-RAY SOCIETY
Secretary, Dr. T. A. Pitts, Baptist Hospital, Columbia, S. C. Meets in Charleston first Thursday in November, also with South Carolina State Medical Association.

TENNESSEE RADIOLOGICAL SOCIETY
Secretary, Dr. J. M. Frère, 707 Walnut St., Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

TEXAS RADIOLOGICAL SOCIETY
Secretary, Dr. R. P. O'Bannon, 650 Fifth Ave., Fort Worth 4, Texas. Next meeting, Dallas, Texas, February 3 and 4, 1950.

UNIVERSITY OF MICHIGAN DEPARTMENT OF ROENTGENOLOGY STAFF MEETING
Meets each Monday evening from September to June, at 7 P.M. at University Hospital.

UNIVERSITY OF WISCONSIN RADIOLOGICAL CONFERENCE
Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets first and third Thursdays 4:00 to 5:00 P.M., September to May inclusive. Room 203, Service Memorial Institute, 426 N. Charter St., Madison.

UTAH STATE RADIOLOGICAL SOCIETY
Secretary, Dr. Angus K. Wilson, 343 S. Main St., Salt Lake City 1, Utah. Meets third Wednesday in September, November, January, March and May.

Virginia Radiological Society
Secretary, Dr. P. B. Parsons, Norfolk General Hospital, Norfolk, Va. Meets annually in October.

Washington State Radiological Society
Secretary, Dr. J. H. Walker, 1115 Terry Ave., Seattle 1, Wash. Meets fourth Monday each month, October through May, College Club, Seattle.

Wisconsin Radiological Society
Secretary, Dr. Irving I. Cowan, 425 E. Wisconsin Ave., Milwaukee 2, Wis. Special meetings held during year; annual meeting each spring at Madison, Wis.

X-Ray Study Club of San Francisco
Secretary, Dr. W. F. Reynolds, University of California Hospital, San Francisco. Meets from January to July at Lane Hall, Stanford University Hospital, and from July to December at San Francisco Hospital.

Cuba, Mexico and Central America

Sociedad de Radiología y Fisioterapia de Cuba
President, Dr. J. Manuel Viamonte, Hospital Mercedes, Habana, Cuba. Meets monthly in Habana.

Sociedad Mexicana de Radiologia y Fisioterapia
General Secretary, Dr. D. P. Cossio, Marsella No. 11, Mexico, D. F. Meets first Monday of each month.

Sociedad Radiológica Panameña
Secretary, Dr. L. Arrieta Sanchez, Apartado No. 86 Panama, R. de P. Meets monthly in a department of radiology of a local hospital, chosen at preceding meeting.

British Empire

British Institute of Radiology Incorporated with the Röntgen Society
Ordinary meeting, on the Thursday preceding the third Friday, October to May at 8:15 P.M.
Medical Members' meeting, on third Friday in each month at 5:00 P.M., 32 Welbeck St., London, W 1.

Faculty of Radiologists
Honorary Secretary, Dr. J. F. Bromley, 45, Lincoln's Inn Fields, London, W.C.2, England.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets third Friday each month at 4:45 P.M. at the Royal Society of Medicine, 1 Wimpole St., London.

Canadian Association of Radiologists
Honorary Secretary, Dr. E. M. Crawford, 1535 Sherbrooke St., West, Montreal 26, Que. Meetings January and June.

Section of Radiology, Canadian Medical Association
Secretary, Dr. C. M. Jones, Inglis St., Ext. Halifax, N. S.

Société Canadienne-Française d'Electrologie et de Radiologie Médicales
Secretary, Dr. Origéne Dufresne, 4120 Ontario St., East, Montreal, P. Q.

Australian and New Zealand Association of Radiologists
Honorary Secretary, Dr. Alan R. Colwell, 135 Macquarie St., Sydney, N.S.W.
Honorary Secretaries, State Branches:
New South Wales, Dr. E. W. Frecker, 135 Macquarie St., Sydney.
Victoria, Dr. T. I. Tyrer, 3 Lockerbie Court, East St. Kilda.
Queensland, Dr. J. Adam, 131 Wickham Terrace, Brisbane.
South Australia, Dr. R. de G. Burnard, 170 North Terrace, Adelaide.
Western Australia, Dr. A. M. Nelson, 179-B St. Georges Terrace, Perth.
New Zealand, Dr. E. G. Lynch, 12 Bolton St., Wellington.

South America

Asociacion Argentina de Radiologia
Secretary, Dr. Lidio G. Mocsa, Avda. Gral Paz 151, Córdoba, Argentina. Meetings held monthly.

Sociedad Argentina de Radiologia
Secretary, Dr. Guido Gotta, Buenos Aires, Argentina. Meetings are held monthly.

Sociedad Argentina de Radiología, Filial del Litoral
President, Dr. Francisco P. Cifarelli. Meets monthly second Wednesday, 7:00 P.M., 663 Italia St., Rosario.

Sociedade Brasileira de Radiologia Medica
Secretary, Dr. Nicola Caminha, Av. Mem de Sa, Rio de Janeiro, Brazil. Meets monthly, except during January, February and March.

Sociedade Brasileira de Radioterapia
Secretary, Dr. Oscar Rocha von Pfuhl, Av. Brigadeiro Luiz Antonio, 644 São Paulo, Brazil. Meets monthly on second Wednesday at 9 P.M. in São Paulo at Av. Brigadeiro Luiz Antonio, 644.

Sociedad Peruana de Radiologia
Secretary, Dr. Julio Bedoya Paredes, Apartado, 2306, Lima, Peru. Meets monthly except during January, February and March, at Asociación Médica Peruana "Daniel A. Carrión," Villalta, 218, Lima.

Sociedad de Radiologica, Cancerologia y Fisica Medica del Uruguay
Secretary, Dr. Arias Bellini.

Continental Europe

Société Belge de Radiologie
General Secretary, Dr. S. Masy, 111 Avenue des Alliés, Louvain, Belgium. Meets monthly, second Sunday at Maison des Médecins, Brussels.

Ceskoslovenská společnost pro röntgenologii a radiologii v Praze
Secretary, Dr. Roman Bláha, Praha XII, stát. nemocnice, Czechoslovakia. Meets monthly except during July, August, and September. Annual general meeting.

Polish Society of Radiology
Secretary, Dr. L. Zgliczynski, 59 Nowogrodzka St., Warsaw, Poland.

Gdansk Section, Polish Society of Radiology
Secretary, Dr. A. Smigielska, Akademia Lekarska, Gdansk. Meets monthly last Sunday at 10.30, X-Ray Dept., Akademia Gdansk.

Warsaw Section, Polish Society of Radiology
Secretary, Dr. L. Zgliczynski, 59 Nowogrodzka St., Warsaw, Poland. Meets monthly.

Societatea Romana de Radiologie si Electrologie
Secretary, Dr. Oscar Meller, Str. Banual Mărăcine, 30, S. I., Bucuresti, Roumania. Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad. USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson. Meets annually.

Leningrad Roentgen Ray Society
Secretaries, Drs. S. G. Simonson and G. A. Gusterin. Meets monthly, first Monday at 8 o'clock, State Institute of Roentgenology and Radiology, Leningrad.

Moscow Roentgen Ray Society
Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky. Meets monthly, first Monday, 8 P.M.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association.

Sociedad Espanola de Radiologia y Electrologia
Secretary, Dr. J. Martin-Crespo, Fuencarral, 7. Madrid, Spain. Meets monthly in Madrid.

Schweizerische Röntgen-Gesellschaft (Société Suisse de Radiologie)
Secretary, Dr. Max Hopf, Effingerstrasse 47, Bern, Switzerland.

Societa Italiana di Radiologia Medica
Secretary, Prof. Mario Ponzio, Ospedale Maurizianc. Torino, Italy. Meets biannually.

ROCKY MOUNTAIN RADIOLOGICAL SOCIETY

The Rocky Mountain Radiological Society is holding its Mid-Summer Radiological Conference at the Shirley-Savoy Hotel, Denver, Colorado, August 17–19, 1950. The program committee is arranging an excellent program. The guest speakers and their subjects (as they appear on the program) are as follows:

1. Dr. George F. Lull, Secretary and General Manager, American Medical Association, Chicago, Illinois:
   a. Medical Economic Policies of the American Medical Association.
2. Dr. Eugene P. Pendergrass, Philadelphia, Pennsylvania:
   a. Diagnosis of Cancer of the Breast and Comments Concerning the Role of Radiation in Its Treatment, and the Effects of Hormones on Breast Cancer.
   b. Meningiomas.
   c. Certain Considerations of the Roentgen Examination in the Diagnosis of Chest Lesions.
3. Dr. Orville Meland, Los Angeles, California:
   a. Carcinoma of the Larynx.
   b. Radiodermatitis Resulting from Uncontrolled Fluoroscopy.
4. Dr. Kent Linblom, Carolina Hospital, Stockholm, Sweden:
   a. Arthrography of the Knee.
   b. Myelography and Disc Puncture.
   c. Nervous Disturbances of the Urinary Bladder.
5. Dr. U. V. Portmann, President of the American Roentgen Ray Society, Cleveland, Ohio:
   a. Cancer of the Breast; Classifying Cases and Manifestations of Incurability.
   b. Radiotherapy for Some Non-malignant Conditions.
   c. Contact Roentgen Therapy for Superficial Lesions.

There are other very interesting papers being arranged.

All physicians interested in radiology are urged to attend this conference. Radiologists should plan their vacation to come to Colorado and participate in this excellent program. There is no registration fee.

SOCIEDAD RADIOLÓGICA PANAMEÑA

At a recent meeting held in Panama City, Republic of Panama, a society of radiologists was formed under the name of Sociedad Radiológica Panameña. The first meeting was held on November 8, 1949, at which time the constitution and by-laws of the Society were approved. The following officers were elected:

President, Dr. J. J. Vallarino; *Vice-President*, Dr. Ernesto Zubieta; *Secretary and Editor*, Dr. Luis Arrieta Sánchez; *Treasurer*, Dr. Roberto Sandoval. Meetings are held monthly in the departments of radiology of the local hospitals, the place of meeting being agreed upon at the preceding session.

ARIZONA ASSOCIATION OF PATHOLOGISTS AND RADIOLOGISTS

At the recent meeting of the Arizona Association of Pathologists and Radiologists held on May 1, 1950, the following officers were elected for the coming year: *President*, Dr. Maurice R. Richter, Phoenix; *Vice-President*, Dr. Ralph H. Fuller, Tucson; *Secretary-Treasurer*, Dr. R. Lee Foster, Phoenix.

GEORGIA RADIOLOGICAL SOCIETY

The annual meeting of the Georgia Radiological Society was held in Macon, Georgia, on April 19, 1950. The following officers were elected for the coming year: *President*, Dr. J. J. Collins, Thomasville; *Vice-President*, Dr. Max Mass, Macon; *Secretary*, Dr. R. C. Pendergrass, Americus. Dr. J. J. Clark of Atlanta was elected Counselor of the American College of Radiology. Dr. J. M. Dell, Jr., Gainesville, Florida, was the guest speaker. His subject was "The Necessity of a Radiologist Being a Good Clinician."

TENNESSEE RADIOLOGICAL SOCIETY

At the recent annual meeting of the Tennessee Radiological Society, held on April 12, 1950, at the Hotel Peabody in Memphis, Tennessee, the following officers were elected for the coming year: *President*,

Dr. Walter W. Robinson, Memphis; *Vice-President*, Dr. Walter D. Hankins, Johnson City; *Secretary-Treasurer*, Dr. J. Marsh Frère, Chattanooga. The guest speaker at the meeting was Dr. William B. Seaman of St. Louis, Missouri.

KAPPA DELTA AWARD FOR RESEARCH IN ORTHOPAEDIC SURGERY

A prize of $1000.00, donated by the Kappa Delta Sorority, is awarded annually by the American Academy of Orthopaedic Surgeons for the best research done in orthopaedic surgery or a related scientific field by an individual in the United States. The second award, for the year 1950, will be presented at the eighteenth annual convention of the Academy in Chicago, January 31, 1951. Researchers interested in competing for this prize are requested to secure further information from Dr. R. Beverly Raney, Duke Hospital, Durham, North Carolina, Chairman of the Award Committee for 1950.

AWARD OF FELLOWSHIP IN PEDIATRIC ROENTGENOLOGY

Dr. Donald K. Bailey, Cincinnati, Ohio, has been awarded the recently established Fellowship in Pediatric Roentgenology in the Department of Radiology of the University of Cincinnati College of Medicine. The fellowship will be awarded annually for a term of one year by the Department of Radiology for study in the Department of Roentgenology of the Children's Hospital of Cincinnati. Dr. Bailey will begin his studies July 1, 1950.

BOOK REVIEWS

Books sent for review are acknowledged under: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interest of our readers as space permits.

SURFACE AND RADIOLOGICAL ANATOMY. For Students and General Practitioners. By A. B. Appleton, M.A., M.D. (Cantab.), Professor of Anatomy, University of London, etc.; W. J. Hamilton, M.D., D.Sc., F.R.S.E., Professor of Anatomy, University of London, etc.; and G. Simon, M.D., B.Ch., D.M.R.E. (Cantab.), Demonstrator of Radiological Anatomy, Medical College of St. Bartholomew's Hospital, etc. Third edition. Cloth. Price, $9.00. Pp. 332, with 390 illustrations. Baltimore: The Williams & Wilkins Company, 1949.

The aim of this book, as stated in the preface to the first edition, is to provide an introduction to the study of features which are accessible to an examination in the living subject. It succeeds admirably in this aim and to a greater extent in this than in previous editions. Noteworthy features are the wealth of excellent roentgenograms so chosen as to illustrate particularly well those features of skeleton and viscera which cannot be ascertained in the dissecting room. The various regional photographs of living subjects are good, and their combination with drawings of dissections or other anatomical illustrations of the same regions are especially instructive. This is a valuable textbook, one which fills a need not met by the usual textbooks of anatomy.

Criticisms which can be made are essentially minor. In a book of this nature, the text and material must be concise and to some extent dogmatic. The danger is that conciseness may be carried too far. For example, the description of cerebral cortex (page 14) serves no useful purpose. Relatively few discrepancies were noted. On page 32, the text refers to the fact that lateral to the acromion process, the shoulder has a rounded contour produced by the deltoid muscle and the underlying greater tuberosity of the humerus. But in Figure 27, a label indicates a surface elevation formed by the head of the humerus.

The authors are to be congratulated on the excellence of their publication.

ERNEST GARDNER, M.D.

HOW TO BECOME A DOCTOR. A Complete Guide to the Study of Medicine, Dentistry, Pharmacy, Veterinarian Medicine, Occupational Therapy, Chiropody and Foot Surgery, Optometry, Hospital Administration, Medical Illustration, and the Sciences. By George R. Moon, A.B., M.A., Examiner and Recorder, University of Illinois, Colleges of Medicine, Dentistry and Pharmacy. Cloth. Price, $2.00. Pp. 131. Philadelphia: The Blakiston Company, 1949.

This book of 131 pages, written by Mr. George R. Moon, Examiner and Recorder of the University of Illinois Colleges of Medicine, Dentistry and Pharmacy, should be of great use to anyone who hopes to study medicine or enter one of the closely allied fields. It gives in an authoritative and condensed form the details concerning admission to a medical school and suggests how one's chances of being accepted may be improved. Furthermore, some of the pitfalls which may lead to failure, after admission to the medical school, are emphasized.

The author states that 90 to 95 per cent of all students who enroll as freshmen will ultimately earn the M.D. degree. This reflects the amount of time and care which is given by committees on admission. The most perplexing admission problem at present, however, is not keeping out the inferior prospects but the inability of medical schools to admit well qualified students on account of the strict limitation of the size of first year classes. While the reviewer does not advocate that all medical schools greatly increase the number of freshmen accepted each year, it is his opinion that some institutions with adequate facilities should be strongly urged to increase their enrollment.

Of special interest to all teachers of medicine is the chapter with the title "Special Problems of the Medical Student." The author summarizes these as the increased cost of medical fees and books as compared to training in other fields, the diminished opportunity to do outside work, and the special health hazards. He does not consider that other personal problems such as marriage differ widely from any other group of college students.

The author gives considerable space to an analysis of why students in medicine fail. In his opinion, it is because of outside factors such as violent love affairs, family quarrels or mishaps, too much time devoted to outside employment, improper living and study conditions, and problems of health such as nervous tension, worry, and loss of interest and enthusiasm sufficient enough to carry them through the long grind of medical school. In general, the reviewer is in accord with the views expressed. A medical student at the beginning of his career should be told that there is nothing in the study of medicine which is especially difficult to understand. A person of even ordinary intelligence is likely to succeed if two things are clearly appreciated: first, he must work intelligently and persistently each day, and not study solely in spurts. After all, medicine is too complex a subject to master in large blocs the night before an examination. Second, and most important of all, the student must have an intense, possessing and genuine desire to become a physician regardless of the obstacles, real and spurious, which may cross his path.

The author is to be commended for making such information available as is presented in this book. Certainly it deserves the careful perusal of all prospective medical students. They will find much in its contents which will serve as a reliable guide for gaining admission to a medical school, and many helpful suggestions concerning their work as medical students.

Cyrus C. Sturgis, M.D.

Roentgen Diagnosis of Diseases of the Skull. (Annals of Roentgenology, Volume XIX.) By Max Ritvo, M.D., Assistant Professor of Radiology, Harvard Medical School; Instructor in Radiology, Tufts Medical School, Boston, Massachusetts; Director, Department of Radiology, Boston City Hospital; Associate in Radiology, Beth Israel Hospital, Boston. Foreword by George W. Holmes, M.D. Cloth. Price, $16.00. Pp. 409, with 466 illustrations. New York: Paul B. Hoeber, Inc., 1949.

The Annals of Roentgenology have added new laurels to their Monographic Atlases in producing the nineteenth volume on "The Roentgen Diagnosis of Diseases of the Skull" by Dr. Max Ritvo, Assistant Professor of Radiology at Harvard Medical School. The author has ably fulfilled his stated objective "to make readily available a collection of roentgenograms illustrative of the various anomalies and pathologic processes of the skull that may be demonstrable by roentgen methods." The publisher has done an excellent job of reproducing the roentgenograms. They have the appearance of the original films. The detail is superior and the labeling of the illustrations is neat, easy to read and not too numerous to be burdensome. The legends are concise and meaty.

A complete and detailed index of all the material is included at the end of the book. In addition, at the conclusion of each chapter and grouped under the disorders that have been discussed is a handy list of the more recent and comprehensive references on those particular subjects. All in all, the general arrangement is outstanding and goes a long way toward making the Atlas a practical and speedy reference monograph.

There are nine well balanced chapters with the following headings: The Roentgenologic Examination of the Skull; Congenital Hereditary, and Developmental Anomalies; Traumatic and Postoperative Changes; Infections; Nutritional, Endocrine, and Metabolic Disturbances; Roentgen Study of the Fetal Skull During Pregnancy; Intracranial Calcifications: Foreign Bodies: Intracranial Accumulations of Iodized Oil: Intraocular Calcifications; Neoplasms; Cerebral Angiography.

The author has justly emphasized the value of obtaining films of excellent quality and the necessity of examining the skull in various positions. He has also stressed the fact that a detailed knowledge of the anatomy of the skull and its appearance on the roentgenograms is required for the proper interpretation. He wisely insists that the radiologist obtain a history from each patient prior to the examination in order that he may have the essential clinical background. Throughout the book the descriptions of the various disorders are enhanced by a brief clinical discussion so that a well rounded picture is presented without having to refer to other sources. Not only are the common disease processes presented, but also the rare and the newly recognized disorders together with present day concepts of them.

Over a dozen sections within the various chapters were written in collaboration with A. Price Heusner, M.D., a neurological surgeon. This has strengthened the clinical character of the discussions. It also presents the surgical viewpoint and makes this volume of more value not only to radiologists, neurological

surgeons, neurologists and internists, but also to all who are interested in the disorders of the skull and its contents. In the preparation of this book the author has rendered an outstanding service.

Wendell G. Scott, M.D.

The Bronchus. By S. Di Rienzo, M.D., Assistant Professor of Radiology and Physiotherapy, Chief of the Radiology Department of the Institute of Cancer, The University of Córdoba, Argentina. Translated by Thomas A. Hughes, M.D. Foreword by Richard H. Overholt, M.D. Cloth. Price, $10.75. Pp. 332, with 466 illustrations. Springfield, Illinois: Charles C Thomas, 1949.

In this monograph, Professor Di Rienzo has reviewed his extensive experience in the roentgenographic study of the bronchi and has presented several new concepts of the physiology and pathology of the tracheobronchial tree.

Discussing first the anatomy and histology of the respiratory tract, he deviates little from the generally accepted facts concerning the structure and divisions of the tracheobronchial tree. A classification of the bronchial arborization is offered, but does not appear to be of any more practical value than those classifications already in general use. Discussions of the use of the plain roentgenogram and tomographic films of the chest are brief; the bronchographic method employing iodized oil is the subject of the major portion of the volume. The author has devised an exacting but complete method of "serial study" of the bronchi. In convincing fashion he illustrates the incompleteness and the often fallacious findings of the usual methods of bronchography, and shows by means of beautiful detail films the superiority of serial observations of the bronchi during filling. Applying the usual technique of injection of the opaque oil, he employs the fluoroscope throughout the procedure, a special table allowing fluoroscopic visualization of the flow of the medium while the patient is placed in suitable attitudes to insure filling of all portions of the bronchial system. Films are exposed as necessary for detail of interesting areas noted fluoroscopically. This method of study obviously requires a cooperative patient, trained technical personnel, unlimited time, and a patient radiologist.

In addition to the exact anatomic detail obtained by this technique, the physiology (normal and pathologic) of the bronchi can be demonstrated, as evidenced by variations in the caliber of the bronchi, peristaltic waves, and the actions of the branch sphincters. Thus, in many phases of respiration and even during the act of coughing, the action of the bronchial components may be studied. The author's interpretation of many of the forms of variation in filling and dynamic action of the bronchi are interesting and may stimulate other radiologists to detect these signs of bronchial and pulmonary disease.

Of particular interest is the study of coughing, which Di Rienzo believes is a dynamic act of the bronchial mucosa which "expulses the air or secretions by means of a peristaltic wave originating in the fine bronchi and which ends in the vocal cords accompanied by an harmonic movement of the functional sphincters." The act of coughing is shown by his films to be altered in bronchiectasis and other diseases.

Subsequent chapters of the volume contain case studies of bronchopulmonary malformations, bronchiectasis, emphysema, asthma, bronchogenic carcinoma, echinococcus cystic disease of the lung, and lung abscess. Numerous roentgenograms correlate the clinical history, the routine chest film findings and the results of tomographic and serial bronchographic study.

The entire work is a monument to the patience, initiative, and scientific curiosity of the author, and it is unfortunate that a rather imperfect English translation persistently annoys the reader. Despite this very minor criticism, the volume should be read by all radiologists. It represents a fine reference source for roentgenographic anatomy of the bronchial tree and also serves as an atlas of bronchial disease as revealed by the bronchogram. Every radiologist who reads this monograph will be inspired to perform more careful bronchographic studies in the future.

Harold Fulton, M.D.

Photoradiography in Search of Tuberculosis. By David Zacks, M.D., Chief of Clinics, Massachusetts Department of Public Health. Cloth. Price, $5.00. Pp. 297, with 270 illustrations and numerous tables. Baltimore: The Williams & Wilkins Company, 1949.

The detection of tuberculosis and other intrathoracic lesions in the population at large by the mass survey method using the roentgen-ray screening method has become such an impor-

tant part of our Public Health Program that detailed descriptions of the procedure, its utility and the problems encountered are most welcome. The author of this book, who is the Chief of Clinics of the Massachusetts Department of Public Health, presents his impressions after twenty years of service in the hunt for tuberculosis. He cites the 80 per cent ten year mortality in symptomatic tuberculosis to illustrate the need for diagnosis before clinical symptoms appear. There is no doubt in his mind that the miniature film method for screening the population is by far the most utilitarian procedure.

The book contains valuable information on the organization of mass surveys, the details of costs, personnel and techniques and a large amount of material concerning promotion and educational methods. The author expounds the problems of the photoradiograph both as to its production and interpretation. He obviously prefers the 4 by 5 inch film, although in his own illustrations the latter suffer by comparison with the reproductions of the 70 mm. size. He advocates examination without disrobing although fully aware of the difficulties occasioned by the shadows of opaque substance in the clothes.

Excessive over-reading of the small film is deplored especially because of the psychic trauma to the individual and the increased expense. He believes double reading is impractical. The principle that the miniature film is purely and simply a screening rather than a diagnostic method is pursued throughout; the full size film is made by the same team which is surveying the population and is used for more specific diagnosis.

The text is accompanied by an atlas of roentgenograms in which the miniature films are reproduced in their original size while segments of the large films, designed to show the area under consideration, are moderately reduced in size. The illustrations include a series of cases of minimal tuberculosis with repeated studies demonstrating some of the progression and regression of typical lesions. Some 230 films illustrating the normal artefacts, unimportant shadows, tuberculosis, non-tuberculous pulmonary lesions and cardiac conditions are included. In many of these both the original photoradiograph and the follow-up 14 by 17 inch roentgenogram are shown. The reproductions are, unfortunately, rather lacking in contrast, but in most cases they demonstrate well the lesion which the author has in mind. The atlas covers reasonably well the broad gamut of lesions encountered during mass chest surveys. There may be some criticism of the inclusion of many unproved cases, especially among the group of heterogeneous round shadows so frequently encountered in chest surveys, but the author's purpose to illustrate many types of abnormalities is well served.

On the whole, this is a sound, well written presentation of the advantages and difficulties of the mass roentgen-ray survey method using miniature film. It should be both interesting and valuable to all who are concerned with such procedures.

Leo G. Rigler, M.D.

Exploration Radiologique de l'Appareil Urinaire Inferieur. (Vessie—Urètre—Prostate.) By Bernard Fey, Fernand Stobbaerts, Pierre Truchot, and Georges Wolfromm, with the collaboration of Léonce Sabadini and others. Paper. Price, 2500 fr. Pp. 291, with 293 illustrations. Paris: Masson et Cie., 1949.

The roentgenological exploration of the lower urinary tract is not a new thing in France, whose radiologists have made large use of urography and have contributed much to its evolution. Cystography, especially by the double contrast method, has been developed in France, and endoscopy has been highly satisfactory. Emphasis is placed upon the fact that in cystography errors of interpretation concerning vesical tumors occur frequently, and that there is a certain uncertainty in surgery of diverticulitis. Cystoscopy alone gives insufficient data.

The authors stress the need for collaboration of the urologist and the radiologist in urographic studies. The various contrast liquids employed included iodine and sodium bromide, a colloidal suspension of gélobarine, lipiodol and the organic iodides of the type of tenebryl, abrodil, etc., as well as a colloidal suspension of thorium dioxide. They have employed not only simple roentgenographic exploration of the urinary tract and urethrocystography by ordinary technique but also combinations of technique, particularly the somewhat difficult contrast-micturition method. The first part of the book is technical; the second part deals with pathological findings. The illustrations are exceptionally good and well reproduced.

James T. Case, M.D.

ABSTRACTS OF RADIOLOGICAL LITERATURE

Department Editor: T. LEUCUTIA, M. D., Harper Hospital, Detroit 1, Michigan

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ROENTGEN DIAGNOSIS

HEAD

STENHOUSE, DAVID. Plain radiography of the skull in the diagnosis of intracranial tumours. *Brit. J. Radiol.*, June, 1948, *21*, 287–300.

Plain roentgenography of the skull is of value in the diagnosis of intracranial tumors despite its comparative inaccuracy when compared with such specialized procedures as pneumography. Since highly technical procedures can be carried out only in centralized units, this analysis was done to determine the value of plain roentgenography. Various authors have reported a percentage accuracy from 8 to 37 per cent with this method of examination. Of 200 cases in this report, 30.5 per cent showed signs of localizing character and 22.5 per cent showed signs of increased intracranial tension. The following criteria were used: (1) histopathological verification of the diagnosis; (2) site of tumor verified at postmortem or operation; (3) previous roentgenogram of the skull. A table is presented showing the percentage incidence of various types of tumor. The extra cerebral group 57.8 per cent showed localizing signs and in the intracerebral group 17.6 per cent showed localizing signs.

Changes in the sella turcica may result from tumor in or near the sella or those distant from the sella. These changes are discussed and do not differ markedly in infra- and supratentorial lesions.

A definite correlation was demonstrated between the degree of hydrocephalus and the relationship of the anterior end of the third ventricle to the sella and the degree of destruction of the dorsum sellae. The encephalographic ratio was used as a measure of the degree of hydrocephalus.

Signs of increased intracranial tension in addition to sellar changes are most commonly observed in the form of separation of the sutures and increased convolutional markings. Attention has been drawn to increase in the size of the occipital emissary veins in some cases. Lack of definition of the lesser wings of the sphenoid is sometimes present with sphenoidal ridge meningiomas. These signs of increased pressure are limited by their being: (1) common to all causes of increased tension—not just those associated with tumor; (2) the increased tension must have been present for at least six months before being capable of detection; and (3) they do not localize a tumor if present.

Localizing signs are discussed. The lateral and sagittal pineal shifts are evaluated, the former being ascertained more readily and easily than the latter. Approximately 50 per cent of routinely examined skulls show calcification of the pineal gland. The lateral pineal shift may not occur in the presence of tumor: (1) if the tumor is situated in the posterior fossa; (2) if it is too small; (3) if the tumor is present bilaterally, exerting equal pressures; and (4) if the tumor is small and supratentorially placed in the midline. The sagittal pineal shift occurs in a smaller percentage of cases but is of considerable value in localizing the lesion if present. This type of shift is almost exclusively caused by supratentorial lesions.

Calcification, bone erosion, new bone formation, and vascular markings as evidence of intracranial tumor in plain skull roentgenography and the tumors which produce them are also discussed.—*K. L. Krabbenhoft, M.D.*

HURXTHAL, LEWIS M., and YOUNGHUSBAND, OMAR Z. Diagnosis of hypopituitarism associated with chromophobe tumor (presumed or verified). *Radiology*, Feb., 1949, *52*, 179–185.

Pituitary chromophobe tumors clinically present signs and symptoms which result from pressure upon or extension to adjacent areas of the brain or as a result of hormonal deficiency from involvement of the pituitary gland.

Visual symptoms such as blurring, reduction of visual acuity or partial loss of sight are usually the first symptoms of which the patient complains. Perhaps the most frequent symptom of chromophobe tumors in females under the age of forty-five is amenorrhea, and it may be stated generally that without this symptom the existence of a chromphobe tumor is unlikely. The onset of menopause without symptoms of menopause should suggest the need for roentgen examination of the skull to determine the presence or absence of an enlarged sella turcica. Other important symptoms are headache, easy fatigability, loss of sexual hair and loss of libido and potentia in the male. A normocytic type of anemia which fails to respond to iron may also be seen in hypopituitarism. Low basal metabolic rates, averaging around minus 20 per cent are not uncommon, but in contrast to hypothyroidism the patient is mentally alert

and exhibits a smooth soft skin. The blood cholesterol is usually within normal limits.

Symptoms which simulate disease of the thyroid, gonads, and adrenals may result from hypopituitarism. In these, tests of thyroid, gonadal and adrenal function, especially the determination of the urinary excretion of 17-ketosteroids and the adrenal water test, as well as studies of carbohydrate metabolism aid in differentiation.

Early diagnosis of chromophobe tumors is dependent upon careful investigation of all cases which show an enlarged sella turcica on roentgen examination. Especially important also are studies of the visual fields and the determination of visual acuity.

In the treatment of hypopituitarism associated with chromophobe tumors, the authors believe that early irradiation is justified whenever there is reasonable evidence of early hormonal deficiency and certainly when there is a suspicion of visual change. In their series of 172 cases, 81 had primary surgical treatment; 85 received roentgen therapy and in 2, no treatment was directed towards the tumor. Medically the treatment is one of replacement therapy to attempt to alleviate the gonadal, adrenal and thyroid deficiencies respectively with testosterone parenterally, with desoxycorticosterone either parenterally or by implantation of pellets and with the oral administration of thyroid extract.—*G. Lavner, M.D.*

Horrax, Gilbert. The diagnosis and treatment of pineal tumors. *Radiology*, Feb., 1949, *52*, 186–192.

Pineal tumors are rare. The symptoms produced result from pressure on neighboring structures. Compression of the aqueduct of Sylvius results in varying degrees of internal hydrocephalus, with associated headaches and vomiting. Other less common symptoms are failing vision, blindness, unsteadiness and staggering, excessive thirst and unusually large urinary output. Pressure on the adjacent corpora quadrigemina give fairly characteristic eye signs, namely, loss of conjugate movement of the eyeballs above the horizontal plane and loss of pupillary reaction to light in the presence of normal or nearly normal visual acuity. A rarer finding in pineal tumors is the presence of premature sexual maturity, pubertas praecox.

A positive diagnosis of a pineal tumor is made by ventriculography. Air studies demonstrate dilated lateral ventricles, dilatation of the anterior portion of the third ventricle and a filling defect in the posterior portion of the third ventricle due to projection of the anterior portion of the tumor.

The treatment of pineal tumors is primarily roentgen therapy, unless critical existing circumstances demand immediate surgery. Prior to roentgen therapy the author advises a preliminary right subtemporal decompression to alleviate symptoms of increased intracranial pressure. After a week or ten days, 3,600 to 4,000 r is delivered to each temporal region, giving a total tumor dose of about 1,850 to 2,000 r. If this fails to cause response a second similar series is given, although a single series is usually sufficient. If there is no response after two or possibly three courses of roentgen therapy, the tumor must be removed surgically. —*G. Lavner, M.D.*

Tamari, M. J., and O'Neil, J. J. Mucoceles. *J. Laryng. & Otol.*, Jan., 1949, *63*, 24–30.

Two cases of mucocele of the frontal sinus and one case of mucocele of the maxillary antrum are presented. A fourth case is included in which the preoperative diagnosis was mucocele but the operative and pathological findings were carcinoma.

On the basis of these cases the authors advance their explanation of the pathogenesis of mucoceles. A submucosal injury, either traumatic, hemorrhagic or infectious, causes an elevation of the mucosa by an accumulation of exudate beneath it. The mucosa is herniated toward the center of the sinus cavity until ultimately the pressure of the herniated mass is exerted on the neighboring bone and the characteristic changes are produced.—*W. H. Granger, M.D.*

Uhr, Nathaniel, and Churg, Jacob. Hypertrophic osteoarthropathy; report of a case associated with a chordoma of the base of the skull and lymphangitic pulmonary metastases. *Ann. Int. Med.*, Oct., 1949, *31*, 681–691.

Metastasizing chordomas of the base of the skull are not at all uncommon. Faust *et al.* quote Mabrey's tabulation of 10 such instances among 27 autopsied cases of spheno-occipital chordoma, with involvement of lymph nodes, lungs, liver and other organs. However, even the malignant chordomas have a relatively

slow course and may extend over a period of years. Cases such as presented here, with rapid course and massive "lymphangitic" metastases, must be very rare.

To reconstruct the pathogenesis of the disease, an expanding lesion in the skull first manifested itself in uncontrollable headaches. The headaches subsided spontaneously, perhaps at the time when the tumor broke through into the nasopharynx, thus relieving the tension. It is reasonable to assume that nausea, vomiting and other intestinal symptoms were also an expression of pressure on the brain stem and that their relief can be explained by the same mechanism. The subsequent neurological manifestations were caused not so much by increased intracranial pressure, as by direct pressure upon the brain stem. Infiltration of the nasopharynx accounts for trismus caused by reflex contraction of the internal pterygoid muscle, unilateral impairment of hearing, probably due to edema of the eustachian tube, and torticollis, a manifestation of eleventh nerve involvement. The tumor invaded nasopharyngeal lymphatics, and, bypassing the cervical lymph nodes, metastasized to the chest. The pulmonary involvement produced no chest symptoms for a considerable length of time, during which it was confined to the lymphatics, yet it was accompanied by rapid and extensive hypertrophic osteoarthropathy. The changes in the long bones were typical of the latter condition. They consisted of marked deposition of newly formed bony traveculae under the periosteum and thickening of the periosteum itself. The joints were not examined at autopsy, but roentgenograms demonstrated atrophic changes about the knees and ankles.—*E. J. McDonald, M.D.*

NECK AND CHEST

URBAN, J. A., and ADAIR, F. E. Sclerosing adenosis. *Cancer*, July, 1949, *2*, 625–634.

The authors emphasize the dangers of the misdiagnosis of sclerosing adenosis for adenocarcinoma. Many needless radical mastectomies are done because of this. They review the pathology of sclerosing adenosis and state that it is not "precancerous."—*J. G. Lorman, M.D.*

CRILE, GEORGE, JR., and RUMSEY, E. W. Subacute thyroiditis. *J.A.M.A.*, Feb. 18, 1950, *142*, 458–462.

Subacute thyroiditis has been defined as an acute or chronic inflammation of the thyroid gland, probably initiated by a virus infection and prolonged by a granulomatous reaction to displaced or perverted colloid. Acute and chronic courses have been recognized.

Subacute thyroiditis occurs between the ages of thirty and fifty years. There were only 5 men in the series of 38 cases seen at the Cleveland Clinic between 1946 through 1948. Sore throat, severe pain on swallowing and tenderness of the thyroid are usually noted at the onset. Pain radiating behind the ear, occiput, face or jaw may be the prominent symptom.

Fatigue, weakness, lassitude and temperatures from 101 to 104° F. are usually noted in subacute thyroiditis. Night sweats, chills, loss of weight, nervousness, tremor weakness and palpitation may be observed.

The thyroid gland is enlarged, firm and tender. The pulse rate is elevated in the acute cases and may be normal in the chronic variety. The sedimentation rate is greatly elevated.

In subacute thyroiditis the thyroid gland takes up little or no radioactive iodine. Low uptake with an average of 9.5 per cent compared to from 30 to 50 per cent take-up by normal thyroids and a from 60 to 90 per cent take-up in hyperthyroidism. In difficult cases needle biopsy has proved of considerable value in the diagnosis.

In the past the treatment of subacute thyroiditis has consisted of bed rests, sedatives and ice packs to the thyroid. During the past ten years roentgen therapy has been considered the treatment of choice. Thirty-five patients were treated with total dosage ranging from 250 to 2,000 r, averaging 800 r, given in daily doses of from 100 to 150 r. Recurrences were treated in 5 patients by a second series of four treatments of 150 r. Undesirable after-effects were in 2 patients. One of these, who had received 2,000 r suffered a mild and transitory hypothyroidism. The other patient had a total of 1,750 r, plus 0.5 millicurie of radioactive iodine, a left lobectomy and a short course of propyl thiouracil which resulted in a mild hypothyroidism. The author does not believe that radioactive iodine has any therapeutic value in this disease.—*J. N. Ané, M.D.*

SWEET, RICHARD H. Intrathoracic goiter located in the posterior mediastinum. *Surg., Gynec. & Obst.*, July, 1949, *89*, 57–66.

In the majority of cases when a goiter extends into the thorax, the enlarging gland pushes downward and forward so that its

lowermost portion lies ultimately in the superior mediastinum just beneath the sternum. It is rare in such a condition for the tumor to lie almost completely within the chest. There is usually a large component of the gland in the neck as well. The term substernal goiter used to designate such an arrangement is only partially correct and to speak of such goiters as being intrathoracic is somewhat misleading. In true intrathoracic goiter, on the other hand, the largest diameter of the tumor lies in the mediastinum below the thoracic inlet. The majority of these lie anteriorly but in a few cases the mass descends into the posterior portion of the mediastinum, a situation which has rarely been referred to in the literature. Its importance lies in the fact that such posteriorly placed goiters are often erroneously thought to be primary mediastinal tumors, and in the fact that if they become very large they can be removed only through a thoracotomy incision.

Conclusions. 1. In general, intrathoracic goiters should be removed not only because of the symptoms they may be causing when the patient is first seen but also because as they increase in size the technical difficulty of the operation becomes greater.

2. In order to plan the operation to the best advantage it is important for the surgeon to distinguish between the anterior substernal goiters and those which lie posteriorly. The former can almost invariably be removed through a cervical incision. The latter, on the other hand, may require a thoracotomy if they are unusually large.

3. The suggestion that the descent of a goiter into the posterior mediastinum is caused by the fact that it happens to arise from the posterior or lateral aspects of the thyroid lobe above the lower pole appears to be a reasonable explanation of this relatively infrequent occurrence.—*Mary Frances Vastine, M.D.*

McCort, J. J. Intrathoracic goiter; its incidence, symptomatology, and roentgen diagnosis. *Radiology*, Aug., 1949, *53*, 227–237.

The author reviews a series of 908 thyroidectomies at the Massachusetts General Hospital, in which 3.1 per cent were proved to be intrathoracic goiters. Only those cases in which the major portion of the gland lay within the thorax were considered to be an intrathoracic goiter. This differs from series of other authors in which different criteria were used for classification. Only 1 of the 28 cases was a carcinoma, and in no instances was there a diffuse hyperplasia with exophthalmos. The goiters were all nodular and only 3 had a mild degree of hyperactivity. The majority of the cases were in patients over fifty. The most common complaint was swelling of the neck followed by dyspnea on exertion, cough, dysphasia, dyspnea on lying down, choking sensation and hoarseness. A few patients were asymptomatic and were found in a routine examination. Physical examination showed some enlargement of the thyroid, the goiter moving upward with deglutition. Some showed dilatation of the neck veins. Intrathoracic goiters are located in the superior mediastinum. Some may be behind the trachea, and 3 were found behind the esophagus.

Roentgen examination contributes most information toward a diagnosis. The significant roentgen findings were displacement of the trachea by the mass, the displacement beginning high in the neck, frequently at the larynx, and occasionally compression. The esophagus may be displaced with the trachea. Upward motion of the goiter with swallowing is characteristic. There may be calcification within the goiter. Even though the tumor is nodular the goiter is usually smooth on the roentgenograms. This is probably due to the fact that the lateral margins of the tumor are formed by the veins in the mediastinum or with the tumor hanging in the upright position there is a smoothing out of the nodular margin. There is almost always a reflection of the mediastinal pleura below the goiter. The author recommends surgical removal and treatment since these cases do not respond to radiation therapy.—*J. Levitin, M.D.*

Steinberg, Israel, and Dotter, Charles T. The differentiation of mediastinal tumour and aneurysm: value of angiocardiography. *Brit. J. Radiol.*, Oct., 1949, *22*, 567–572.

Because of the difference in surgical approach, among other reasons, accurate differentiation of a mediastinal aneurysm and other possibly surgically manageable tumors is imperative. Angiocardiography practically always either demonstrates an aneurysm or excludes that possibility. Rarely a clotted canalized lumen exists and the sac is not shown. Collateral circulation is helpful in these cases.

A series of interesting angiocardiograms is presented. The films were made without expensive special apparatus. They were made using a standard stereo cassette changer, ob-

taining two exposures per injection. Cases presented showed that pulsation or lack of it might be associated with either aneurysm or solid tumors. Dilatation of the mid-ascending, and calcification of the ascending were found regularly in luetic aortitis.—*E. F. Lang, M.D.*

ESPINOZA GALARZA, M. Tomography of larynx in disseminated pulmonary tuberculosis. *Dis. of Chest*, July, 1949, *16*, 100–102.

A preliminary study of 10 proved cases of laryngeal tuberculosis was outlined using tomographic illustrations of 4 patients with proved disease. The constant tomographic sign in all cases is the subglottic angle which becomes frankly obtuse, regardless of degree of tuberculous laryngitis; whereas, the normal angle is rectangular.

The author gives specific roentgenographic technique, and suggests that the patient be placed in the prone position for this study.—*Frederick R. Gilmore, M.D.*

GILBERT, J. G., KAUFMAN, B., and MAZZARELLA, L. A. Tracheal tumors in infants and children. *J. Pediat.*, July, 1949, *35*, 63–69.

The authors were able to find only 39 reported cases of tracheal tumors in infants and children, as compared with 488 reported cases in adults. Papillomas comprise about half the reported cases, with fibromas and angiomas next in frequency. The incidence of malignant tracheal tumors in infants is 7.5 per cent as compared with 40 per cent in adults. The commonest site of involvement in children is the upper third. Tumors of the upper third produce symptoms due to involvement of the vocal cords, such as noisy respiration, while those of the lower third lead to atelectasis with wheezing or harsh breath sounds. Those tumors with long pedicles are more productive of symptoms than those with short pedicles.

The differential diagnosis must include laryngismus stridulus, cysts, and laryngeal papillomas.

The authors report 2 cases of their own, both in infants of eleven months. The films of one case are reproduced. These show the presence of a soft tissue tumor mass obscuring the air shadow of the lower trachea. This case proved to be a fibroangiomatous polyp, the other case being a capillary hemangioma.—*Rolfe M. Harvey, M.D.*

MATHESON, IAIN. Foreign bodies in the œsophagus; review of six hundred and two cases. *J. Laryng. & Otol.*, Aug., 1949, *63*, 435–445.

This article is based on 602 cases of esophageal foreign bodies seen in the Endoscopic Unit, St. Giles Hospital, London, since 1936. In 377 cases, a foreign body was removed; in 77 cases a laceration of the esophagus was seen; while in 148 cases a foreign body was not found or removed. In all these 148 cases the foreign body had been located by roentgen methods but passed on into the stomach in the interval before esophagoscopy or was seen on esophagoscopy but passed on into the stomach before it could be grasped.

The age of the patient was under eighteen years in 153 cases and over eighteen in the remaining 449 cases.

In the 377 cases in which a foreign body was found, the site of impaction was in the pyriform fossae in 8 cases (2.0 per cent), in the hypopharynx in 29 cases (7.7 per cent), at the cricopharyngeal sphincter in 225 cases (60 per cent), between the cricopharyngeal and the cardiac sphincters in 72 cases (19.1 per cent), at the cardiac sphincter in 13 cases (3.4 per cent) and in 30 cases (7.8 per cent) the location of the foreign body was not mentioned.

Reasons for an occasional repetition of an esophagoscopy were: (1) failure to remove the foreign body at the first attempt, (2) failure to persuade the patient that there was no foreign body in the esophagus, and (3) desire to inspect the amount of healing of a laceration.

The author thinks a roentgen examination of the chest should be performed in all cases of a suspected esophageal foreign body in children regardless of lack of symptoms. The esophagus of a child appears to be much more tolerant of a foreign body than that of an adult. Two examples are given in which foreign bodies had been present in the esophagus for eight months and for six weeks respectively.

Two deaths have occurred following removal of the foreign body. The first case was that of a forty-two year old man who died of toxic myocarditis and a large abscess in the neck nine days after esophagoscopic removal of a partial denture. The second case was that of a sixty-two year old man who swallowed a piece of mutton bone. A laceration was found in the posterior esophageal wall, but no bone could be seen or felt. Six days after esophagoscopy (nine days after swallowing the mutton bone) he died. At autopsy a triangular piece of bone

which had perforated both sides of the esophagus was found. There was also purulent mediastinitis, bronchopneumonia and a large right-sided pleural effusion.—*W. H. Granger, M.D.*

Holinger, Paul H., Johnston, Kenneth C., and Greengard, Joseph. Congenital anomalies of the esophagus related to esophageal foreign bodies. *Am. J. Dis. Child.*, Oct., 1949, *78*, 467–476.

This paper is an analysis of cases of foreign bodies in the esophagus in which the lodgment of the foreign body was due to a congenital anomaly of the esophagus. Three types of congenital lesions are considered in the discussion: congenitally short esophagus, congenital esophageal stenosis, and stricture of the esophagus which may follow the repair of a congenital esophageal atresia. Differentiation between a congenitally short esophagus and a congenital esophageal stenosis is best made by roentgenographic and esophagoscopic examinations.

The symptomatology of the two types of esophageal congenital stenoses is identical although their roentgenographic appearances differ. Usually no symptoms are present during the first five months of life, when the infants are on a liquid diet. When semisolid foods are added to the diet, feeding problems manifest themselves by slow eating and a reluctance to take anything but liquids. When solids are added to the diet, frequent episodes of temporary obstruction occur with drooling, vomiting of undigested food and loss of weight. Bizarre eating habits develop, with the result that as the child grows older the time used to consume a meal may extend to an hour or more. Finally, episodes of complete obstruction occur which require esophagoscopic removal of a foreign body—a piece of meat, an orange seed, a toy or a coin.

Six cases with illustrative roentgenograms are reported in the paper.—*R. S. Bromer, M.D.*

Bruzzone, P. L., and Bellion, B. Considerazioni clinico-radiologiche sul valore del segno di Minnigerode. (Clinical roentgenographic evaluation of the Minnigerode sign.) *Ann. laring., otol.*, 1949, *48*, 11–20.

The "Minnigerode sign" is a roentgenographic sign diagnostic of early perforation of upper end of the esophagus, secondary to foreign body.

It usually develops within twenty-four to forty-eight hours after history of initial dysphagia. Its initial features are: (1) regional prevertebral soft tissue widening; (2) air within the soft tissue with or without visualization of a foreign body.

It is a valuable roentgenographic sign because it is usually observed earlier than other clinical findings, thus enabling earlier and better planning of treatment.

It was originally described in 1923 by Minnigerode and has been used successfully by other European authors and in 2 recent cases by the current authors.

Anteroposterior and lateral views of the cervical region may suffice. At times, the use of a swallow of barium may aid in diagnosis by showing locally obliterated mucosal pattern and the existence of sinus tract. The presence of air within the apex of the lung must not be confused with the true soft tissue emphysema secondary to perforation.

Indication for immediate surgery should not be based on the above roentgenographic findings but upon clinical findings such as mediastinitis or sepsis.—*C. A. Priviteri, M.D.*

Lanari, Carlos. La tomografía de perfil en el estudio del vértice pulmonar; técnica personal. (Side view tomography in the study of the pulmonary apex; author's technique.) *An. Cáted. de pat. y clín. tuberc.*, 1948, *10*, 54–62.

The author describes a modification of the classical tomography of the chest in the lateral view. The patient is placed with the side to be examined toward the film. The arm is raised horizontally and the shoulder pulled forward, whereas the hand of the opposite side is put on the waist and the shoulder is forced as far back as possible. The correct position is reached when the opposite shoulder projects behind the apex to be examined. In this view there is a slight rotation of the thorax, amounting to an average of 16 degrees.

Two or three sections are made. The zero point corresponds to the spinous processes. In case of large lesions, two sections suffice: the internal passes 1 cm. lateral to the spinous processes, touches lightly the vertebral column and continues anteriorly through the supraclavicular fossa; the external passes 2 cm. farther outward and cuts through the first rib. If the examination is undertaken for the demonstration of apical cavities, three sections are made: at zero, 2 cm. and 4 cm. lateral to the spinous processes. Following thoracoplasties the

first section is made 1 cm. lateral to the spinous processes.

The voltage is increased with 10 to 15 kv. over that used in frontal tomography except in very heavy patients where it is increased more. The technique is relatively simple. The margin of error in selecting the sections rarely exceeds 1 cm.

The author states that the purpose of this technique is to eliminate the interfering shadows cast by the shoulders. The slight rotation of the thorax constitutes no undue inconvenience, there being only little distortion of the roentgen image. Tomograms in the normal and in various pathologic conditions are presented to illustrate the value of the procedure.

In the normal, the Valsalva test produces an increased translucency of the apex which rises above the level of the first rib. In tumors it is possible to study the relationship between the first rib and the apex. In one of the author's cases a hydatid cyst of the apex was successfully removed due to the fact that lateral tomography showed the lesion to be confined within the lung tissue. Although the author himself has no experience, he believes that the method is also of value in neurogenic tumors of the upper chest. In cavities it gives added information supplementary to that obtained in the frontal and oblique views.

Because of these advantages a systematic use of the method is recommended.—*T. Leucutia, M.D.*

Boyden, Edward A. A synthesis of the prevailing patterns of the bronchopulmonary segments in the light of their variations. *Dis. of Chest*, June, 1949, *15*, 657–668.

This is a summary of mapping the arrangement and distribution of the tracheobronchial and vascular trees within both lungs, lobe by lobe, from a composite study of at least fifty or more specimens of each lobe after being dissected or freely injected with colored gelatins. Individually, the various lobes are analyzed with segmental drawings illustrating the statistical variations from the usual bronchial tree with ten major segments on the right and nine on the left.

The author discusses the similarity of this study with that of Jackson and Huber, and suggests minor changes in the disposition of segments. After paying tribute to Brock's fundamental anatomical study which relates the casts of the bronchial tree to the bronchographic appearance, Boyden goes a step farther by identifying both segmental and subsegmental bronchi, their distribution, and variations.—*Frederick R. Gilmore, M.D.*

Duisenberg, Charles E., and Arismendi, Luis. The angiographic demonstration of pulmonary arteriovenous fistula. *Radiology*, July, 1949, *53*, 66–74.

This article gives a tabulated review of 22 cases of pulmonary arteriovenous fistula. The first contrast angiography to diagnose this condition was in 1939, and the first successful surgical removal was in 1942. The signs and symptoms vary greatly, but include in order of frequency: (1) abnormalities noted by roentgenographic examination, (2) cyanosis, (3) polycythemia, (4) clubbing of the fingers, (5) murmur over the affected lung, (6) hemoptysis.

The authors add an additional case showing hemoptysis with excellent angiograms. This patient was successfully operated upon.—*F. H. Squire, M.D.*

Ettinger, Alice, Magendantz, Heinz, and Russo, Edward A. Arteriovenous aneurysm of the lung; case report. *Radiology*, Aug., 1949, *53*, 261–267.

The authors report a case of arteriovenous aneurysm of the lung in a thirty-four year old housewife characterized by several episodes of hemoptysis over a ten year period. On several previous hospitalizations the cause of hemoptysis was not diagnosed.

On the next to last hospital admission all cellular and chemical elements of the patient's blood were increased. On roentgen examination a structureless shadow almost completely obscured the left lung markings and it was thought at first to represent fluid. Bronchographic studies led to a diagnosis of probable atelectasis of the left lower lobe.

On last hospitalization roentgen examinations revealed a 4 by 5 cm. lobulated mass behind the cardiac shadow suspected of being an arteriovenous aneurysm of the lung. Further study by laminagraphy showed two separate small round shadows in the left lower lung field and with spot films taken with the patient performing the Valsalva test a reduction in the shadow was noted to about half its original diameter. At this time the arterial hemoglobin oxygen saturation was markedly diminished at rest. A left lower lobectomy was performed with operative findings and subsequent pathologic

diagnosis that of arteriovenous aneurysm.

The authors discuss the roentgen diagnosis stating a lobulated mass connected at the hilus by band-like vasular shadows should be highly suggestive of arteriovenous aneurysm. In a small number of cases demonstrable pulsation may be detected fluoroscopically. Laminagraphy is frequently helpful, demonstrating connection of the tumor-like shadow with the hilar region. Angiography would seem to be the most conclusive means of establishing the vascular nature of the lesion. Use of the Valsalva test is discussed with its value in change in size of the apparent tumor mass as reported by the authors. In the review of published cases plain films were found to be characteristic in all but 2 cases.

The differential diagnosis includes tumor of the lung.

Additional clinical features are discussed with the principal findings of the syndrome including polycythemia, cyanosis, clubbing of the fingers and toes, repeated hemoptyses, breathlessness, faintness, dizziness and weakness, and a distant bruit or hum in the chest.

The article includes several reproductions of roentgengrams and a clinical table of laboratory studies with an artist's diagrammatic representation of operative findings.—*J. H. Gilmore, M.D.*

Peroncini, José, Bence, Alvaro E., Vaccarezza, Oscar A., and Agüero, José G. Torulosis bronquial y meníngea. (Bronchial and meningeal torulosis.) *An. Cáted. de pat. y clín. tuberc.*, 1948, *10*, 149–156.

The first torula infection in man was observed by Verse in 1914. Since that time not more than 100 cases have been reported in the world medical literature.

The infection is caused by *Torula histolytica* (*Cyrptococcus hominis*). It occurs at any age but is seen more frequently between the ages of twenty and sixty years, the male being attacked twice as often as the female. Its geographic distribution is universal.

It is generally accepted that *Torula histolytica* enters the system via the respiratory route. This explains the frequent pulmonary localization of the disease as well as the fact that even in those cases in which extrapulmonary manifestations dominate the clinical picture nearly always some involvement of the lungs is found on roentgen study.

From the lungs the infection spreads by means of the blood stream to various organs, the nervous system constituting the most favored site of secondary localization.

The symptoms vary considerably. The most common among them are those referable to some involvement of the respiratory apparatus (bronchopulmonary, pulmonary, pleuropulmonary, and pleural) and of the meninges (increased intracranial pressure). Others may result from spreading to the lymphatics, skin, mucosae, and joints, and from general septicemia.

The evolution follows two courses: most patients die within an average of six months (the shortest known survival being 25 days), others survive and continue to have exacerbations and remissions for several years. The question of possible immunity was studied but so far the results remained unsatisfactory.

The diagnosis is based on microscopic demonstration of *Torula histolytica* in biopsied specimens, sputa, urine and especially cerebrospinal fluid, considering the frequent secondary localization to the central nervous system. Verification is made through cultures in artificial media.

The treatment consists in the administration of sodium or potassium iodide, sulfa drugs and various antibiotics. As a rule, it remains ineffectual.

In view of the usually fatal outcome of the disease the authors present the detailed clinical record of a patient who survived five years since the onset of the first symptoms of torula. A review of the literature revealed that there are only 8 cases reported who lived four years or longer.

In the authors' case, that of a man aged thirty-two, the disease was localized to the pulmonary apparatus and the central nervous system. The outstanding roentgen finding of the chest was atelectasis of the left lung. Bronchoscopic examination revealed the presence of a granuloma which blocked the lumen of the left main bronchus and was thus responsible for the atelectasis. Microscopic examination of the biopsy showed *Torula histolytica* which was confirmed by culture. During the course of treatment, signs of meningeal involvement with increased intracranial pressure and ocular manifestations developed. A study of the cerebrospinal fluid revealed the presence of *Torula histolytica*. Following intensive penicillin therapy associated with autovaccines the patient made a complete recovery. There was no further exacerbation of the disease for more

than three years. The roentgenograms of the chest prior to institution of the treatment showing atelectasis of the left lung and four years later showing normal appearance are reproduced.—*T. Leucutia, M.D.*

SELVAAG, OTTO. Erythema multiforme exudativum and pneumonia; some pathogenetic considerations in connection with a case presenting miliary lesions of the lung and increased titer of antistreptolysins and cold agglutinins. *Acta med. Scandinav.*, July, 1949, *135*, 34–39.

A case is presented which demonstrates the simultaneous occurrence of erythema multiforme exudativum and a miliary form of primary atypical pneumonia. This gives rise to differential diagnostic considerations among conditions such as miliary tuberculosis. It is suggested that the miliary pneumonia may be a manifestation of or a result of an enanthema in the deeper air passages.

Cold agglutinins as well as antistreptolysins were both present in pathological amounts, the latter probably being an expression of a concurrent or secondary infection, with hemolytic streptococci.—*Charles Nice, M.D.*

MIDDLEMISS, J. H. Erythema nodosum. *Brit. J. Radiol.*, June, 1949, *22*, 375–383.

Of a group of 124 patients with erythema nodosum, 56 showed pulmonary changes. The patients with pulmonary changes were classified into various groups according to the lung manifestations, and altogether more than one-third of these had biopsies made of the skin lesions for control. All cases showing active pulmonary changes gave a positive tuberculin reaction. The pulmonary changes were grouped as follows:

(1) A primary tuberculous complex was found in 24, all under sixteen years of age.

(2) Glandular enlargement was present in 25 cases; in each instance this was unilateral. This was considered tuberculous in each case, probably with a hidden primary focus. Two of these patients subsequently developed pleural effusion. No case of lymphadenopathy resolved in less than eight months, and in 4 calcification developed in the glands as they diminished in size.

(3) Bilateral active pulmonary tuberculosis was seen in 4 cases. In 1 of these the skin lesions developed on two occasions following administration of sulfonamides.

(4) Plueral effusion was found in 2 patients.

(5) In 1 case with a strongly positive Mantoux reaction, enlarged hila suggesting blocked lymphatics, developed subsequently. This was not thought to be on a tuberculous basis.

Of the remaining 68 cases with no roentgen evidence of active pulmonary changes, 44 had positive tuberculin reactions.

The author concludes that since 77 per cent of this series could be regarded as tuberculous, tuberculosis must be considered in every case of erythema nodosum. In all cases apparently the eruption is a nonspecific allergic phenomenon.—*E. F. Lang, M.D.*

BYRON, F. X., ALLING, M. E., and SAMSON, P. C. Intrathoracic meningocele. *J. Thoracic Surg.*, June, 1949, *18*, 294–303.

Three cases of proved intrathoracic meningocele are presented. In all these cases a preoperative diagnosis of neurofibromatosis of von Recklinghausen was made. This is easily understood because of the typical roentgen findings of a uniformly opaque, well defined, rounded or lobulated mass in the posterior mediastinum and bony absorption of adjacent posterior rib ends and the skin manifestations of neurofibromatosis. These latter were seen in 3 of the 5 cases reported in the literature and 2 of the cases described in this report. The significance of the fact that neurofibromatosis was present in so many of the cases of intrathoracic meningocele is not clear. Short of thoracotomy or thoracostomy, therefore, the only procedure that offers a good chance of differential diagnosis is the intraspinal injection of an opaque medium and positioning of the patient so as to fill, if possible, the suspected meningocele. The demonstration of a spinal fluid block above the level of the meningocele in one case reported in the literature would seem to indicate the presence of an intraspinal lesion and in one of the authors' cases a small intraspinal cyst was also observed. It seems possible that both the meningocele and intraspinal cysts could have arisen at points of congenital weakness of the dura. The treatment by surgical excision is discussed.—*F. M. Reis, M.D.*

SHAW, R. R. Thoracic complications of amebiasis. *Surg., Gynec. & Obst.*, June, 1949, *88*, 753–762.

Hepatic abscesses are common complications of amebic dysentery. These abscesses are best treated by emetine therapy and should not be

treated surgically unless certain indications are present.

Pleuropulmonary complications of hepatic abscesses can in the majority of patients be successfully treated with emetine therapy.

Surgery will be required if: (1) the lung cannot be re-expanded, (2) a bronchobiliary fistula persists, (3) secondary infection occurs, and (4) when damaged pulmonary tissue produces a continued morbid state.

Formal thoracotomies with removal of as much of the products of the infection as possible are preferable to drainage procedures.

Proper surgical intervention should further lower the mortality and morbidity in this disease.—*Mary Frances Vastine, M.D.*

Robbins, Laurence L., and Sniffen, Ronald C. Correlation between the roentgenologic and pathologic findings in chronic pneumonitis of the cholesterol type. *Radiology*, Aug., 1949, *53*, 187–202.

In this increasingly frequent form of chronic pneumonitis there is an interstitial inflammation in which the exudate is largely composed of mononuclear cells filled with cholesterol and cholesterol esters. It is a condition found commonly in the presence of bronchial obstruction and in small localized areas in chronic affections such as bronchiectasis, pulmonary abscess, and tuberculosis.

In the 11 cases treated surgically which are the substance of this report no major bronchial obstruction or significant coexistent lung disease could be demonstrated roentgenologically or anatomically in the area of pneumonitis. Of the 11 cases 10 were males and 1 female and this was in a child of twelve. No characteristic bacteria were found. There was no convincing evidence of nosedrop treatment as a precursor. The treatment was surgical because the lesion could not be differentiated from tumor in some instances and because when the diagnosis was recognized preoperatively it was known that the condition tended to extend rather than to heal.

Roentgenographically the appearance is quite similar or similar enough to be confused with tumor, lung abscess or infarct. Two general classifications of the findings are presented. In 5 cases there was extensive involvement of a lobe and in 6 the lesion was localized to a portion of one or more segments. In the former group some collapse existed, there was a rather homogeneous density and there was no gross evidence of bronchial dilatation.

In the second group where only a portion of a lobe was involved the shadow was seen to lie against the pleura peripherally or along a fissure, the long dimension being parallel with the pleural surface. The margin away from the pleura was rounded or lobulated and sharply defined. Fluoroscopy was helpful in determining the best projection for demonstration of this feature. Occasionally pleural fluid was seen in both groups and sometimes a mild mediastinal or hilar accentuation. Rare cavities were seen but they did not seem to be typical of lung abscess or of bronchiectatic cavities.

In the differential diagnosis it would be impossible to differentiate this from neoplasm on the basis of the collapse of a lobe by roentgen methods alone. The definition of the area of increased density in pneumonitis is ordinarily less sharp than that due to the presence of a primary peripheral tumor or metastatic lesion. The margins are somewhat irregular and lobulated but the lobulations may be larger than those seen in a peripheral tumor. When iodized oil was introduced it was found that several bronchi seemed to end abruptly at the area of increased density rather than one as might be the case in obstruction due to a tumor of a single large bronchus. The hilar lymph node enlargement differed in no way from that due to neoplasm. The chronicity of the disease seems to be the only way to differentiate this from a lung abscess before abscess formation is visible. The lesion is quite similar to that noted in pulmonary infarctions but the lesion in pneumonitis is not so commonly at the junction of two pleural surfaces as in pulmonary infarction and the margins are more sharply defined. Furthermore, in this type of chronic pneumonitis the lesion tends to spread whereas infarction usually, if followed, tends to heal in a relatively short period.

Pathologically the operation specimens reveal contraction of the affected lobe with fibrous adhesions involving all the pleural surfaces, particularly dense at the site of the lesion. The bronchial lymph nodes were enlarged, often reaching a diameter of 2 cm. The disease had a tendency to assume a pyramidal shape fanning out from the hilus with the base at the pleura. It did not adhere strictly to pulmonary segments. At least one pleural surface was always involved but the fissures were not penetrated except in one instance. In early phases of the

process the area of pneumonitis was an intense yellow. As healing progressed the parenchyma became gray and fibrous. Chronic inflammatory changes are seen in the larger bronchi with minimal dilatation. Microscopically large mononuclear cells with foamy cytoplasm and fine droplets are seen with a chronic interstitial pneumonitis soon superimposing. The tissue response was characterized by edema and a lymphocyte and plasma cell infiltration with the lymphocytes frequently aggregated in follicles. The reaction was followed by much collagen and fibrosis. Analysis of the tissues showed values for cholesterol and its esters as high as 24 and 90 times the normal respectively. Pathologically the similarity between this type of pneumonitis and aspiration pneumonia due to paraffin-oil is striking. A clearcut cause for this condition was not apparent from the pathological survey.

The authors state that it is obvious that under some circumstances it will be impossible to differentiate this condition from tumor but a strong suspicion should be suggested in the presence of the above roentgen findings. The authors suggest that the etiological agent may be some obstruction of the smaller bronchi or bronchioles which is so often present but the precursor of this condition of course could be any number of conditions including infection. Apparently the eventual outcome in most cases not surgically handled will be fibrosis in the area of involvement.—*A. J. Present, M.D.*

FREEDMAN, EUGENE, and BILLINGS, JAMES H. Active bronchopulmonary lithiasis. *Radiology*, Aug., 1949, *53*, 203–215.

Seven cases of active bronchopulmonary lithiasis are reported, of which 6 were proved at surgery and subsequent microscopic examination.

The stones may reach the bronchial lumen in either of two ways: (1) An infection with suppuration may develop in the area of the calcific focus, causing mobilization and slow perforation through the bronchial wall of an adjacent and previously "silent" stone. (2) The inspiratory expansion and expiratory collapse of the bronchi and surrounding vascular structures may expose a section of the bronchial wall to the eroding action of an adjacent calcified node.

The majority of broncholiths are due to perforation of calcified tuberculous lymph nodes. Active tuberculosis is rarely accompanied by the expectoration of stone.

During the process of perforation hemorrhage may occur from an exposed blood vessel in the ulcerated bronchial wall or from direct erosion by the stone of a large pulmonary vessel in the hilar region.

Partial or complete obstruction of a bronchus may occur, depending on size and shape of calculi lodged within. Atelectasis, pneumonitis, bronchiectasis and abscess formation usually follow.

The clinical manifestations are manifold and depend greatly on the degree of obstruction and the extent of the secondary inflammatory changes distal to the obstruction.

Active bronchopulmonary lithiasis should be included in the differential diagnoses of every case of bronchial obstruction, pulmonary suppuration and hemorrhage associated with paroxysmal attacks of cough, where the chest roentgenogram shows calcific shadows in the region of consolidated areas.

Bronchoscopy may reveal the calculus within the bronchi or arouse suspicion of one by revealing an ulceration or granulomatous lesion in the bronchial wall. Planigraphy may demonstrate a broncholith perforating the bronchial wall or lying in the lumen of the bronchus.

Easy recognition and treatment of bronchopulmonary lithiasis may prevent the serious complications caused by bronchial obstruction, pulmonary suppuration and hemorrhage.— *R. L. Niehaus, M.D.*

GRAYSON, CHARLES E., and BLUMENFELD, HELEN. "Egg shell" calcifications in silicosis. *Radiology*, Aug., 1949, *53*, 216–226.

The authors reviewed 200 cases of silicosis, in 88 of which there were sufficient data for approximate dust exposure statistics. Thirty-seven cases with egg-shell calcifications were compared with 51 cases having no visible hilar calcifications. The average age and the average time since the earliest exposure were essentially the same in the two groups. Sixty per cent of those having calcifications and 49 per cent of those having no calcifications were without evidence of tuberculosis.

Eight cases of particular interest were those which met the following criteria: (1) history of exposure to silica, (2) roentgenograms showed shell calcifications and nodular pulmonary densities, (3) an autopsy diagnosis of

silicosis was confirmed, and (4) absence of clinical or histological evidence of chronic pulmonary infection. Shell calcifications were found only in lymph nodes but not in lung parenchyma. Sections of the hilar nodes showed that slight fibrosis was the only change seen in the earliest lesions. In more advanced lesions, calcium was found about the periphery of the node but sometimes extended irregularly into the substance of the node. None of the nodes showed any active process suggesting tuberculosis. Sections of the parenchymal pulmonary lesions showed nodules of fibrous tissue in which there was no annular deposit of calcium. Guinea-pig inoculation of portions of lung tissue and hilar nodes showed no demonstrable lesions except fibrosis at the infection site.

The authors conclude that the presence of egg-shell calcifications in lymph nodes indicates silicosis. No other causes have been reported with any reasonable supporting evidence.—*W. H. Granger, M.D.*

Dunner, L., and Bagnall, J. T. Pneumoconiosis in graphite workers. *Brit. J. Radiol.*, Oct., 1949, *22*, 573–579.

"Graphite lung" is a condition marked by by striation, fibrosis, nodulation, large opaque patches, or combinations of those.

One graphite worker with pulmonary changes was subjected to postmortem examination. This revealed definite fibrosis, probably silicotic in origin; scattered pulmonary deposits of graphite; cysts filled with black fluid containing much graphite but no silica.—*E. F. Lang, M.D.*

Vaccarezza, Raúl F., and Soubrié, Alberto. Influencia de la paquipleuritis sobre el valor funcional del pulmón; estudio broncoespirométrico. (Influence of pachypleuritis on the function of the lung; bronchospirometric study.) *An. Cáted. de pat. y clín. tuberc.*, 1948, *10*, 5–23.

The authors performed bronchospirometric studies by Gebauer's intubation in 12 cases of pleural thickening. All except one had active pulmonary tuberculosis at the time of the examination. In 3 cases the pleural thickening was the result of spontaneous pleuritis, while in the other 9 it constituted a sequel to therapeutic pneumothorax.

The following average values were found for the lung of the affected side: oxygen consumption 26.8 per cent, complementary air 26.9 per cent, vital capacity 38.8 per cent, reserve air 38.9 per cent and minute respiratory volume 44.8 per cent. Considering that in 10 of the 12 cases examined the pleural thickening involved the right side, the average bronchospirometric values should have been 53 per cent.

The clinical records of the 12 cases are presented in detail and their respective roentgenograms reproduced.

It is obvious from the above figures that the oxygen consumption undergoes a comparatively greater reduction than the vital capacity and especially the minute respiratory volume. In other words, the function of gaseous diffusion suffers more than the function of ventilation. Björkman attributed this finding to the lessened blood circulation in the affected lung. The authors believe that the extension of the sclerotic process to the entire surface of the lung and the subjacent lung parenchyma impairs the hematosis in a rather large number of the peripheral alveoli. This then proves that the lung has lost its capacity to distend or relax as completely as is the case in deep or forced respiration.—*T. Leucutia, M.D.*

Rottenberg, Louis A., and Golden, Ross. Spontaneous pneumothorax; study of 105 cases. *Radiology*, Aug., 1949, *53*, 157–167.

The authors present a study of 105 consecutive cases of spontaneous pneumothorax to determine its possible relationship to pulmonary tuberculosis. In a review of the literature, the three most important etiological agents in pathogenesis of spontaneous pneumothorax were considered to be pulmonary tuberculosis, congenital vesicles and emphysema. A number of early reports indicated that spontaneous pneumothorax was more or less pathognomonic of tuberculosis in the lungs or pleura, though more recent authors have found little evidence of tuberculosis developing in these cases.

In congenital vesicles there is a persistence of embryonal tissue in the peripheral zone of the lung which does not differentiate into alveoli but instead is changed into cystic areas which enlarge and rupture. Localized emphysema in the form of subpleural bullae appears to be the usually accepted explanation at present for the pathogenesis of simple spontaneous pneumothorax. Air forced from the bases of the lungs into the upper lobes distends and ruptures the elastic fibers of the alveoli. Active, robust men are most likely to overdistend their upper lobes. The bulla is the first require-

ment. The next is a check valve type of mechanism which prevents the return of air from the bulla and finally exertion to rupture the overdistended bulla.

Of the present series 97 cases occurred in apparently healthy individuals. Six cases occurred in patients with already existing tuberculosis. The average age was thirty years, and most of the cases were not associated with severe exertion. The two major symptoms were severe sudden chest pain and dyspnea. Forty-seven per cent had slight to moderate amounts of pleural effusion which was gradually absorbed. This was considered in the past as evidence in favor of tuberculosis. Tension pneumothorax, bilateral pneumothorax and hemopneumothorax are complications which may endanger life.

Fifteen of the authors' cases have been followed five to ten years and 7 followed ten to eighteen years, and in no instance has tuberculosis developed. This study indicates that if tuberculosis is not present at the time the pneumothorax occurred, it is no more likely to develop than in the average individual in the community.—*W. M. Roy, M.D.*

SOLOVAY, JULIUS. Spontaneous hemopneumothorax; etiological considerations and case report. *Radiology*, Aug., 1949, *53*, 256–260.

Trauma, tuberculosis and cancer are not uncommonly responsible for the appearance of blood or bloody fluid with or without air in the pleural cavity. There are other less common causes but on rare occasions hemopneumothorax occurs as a dramatic medical emergency uninitiated by trauma or the usual diseases and under such conditions is called spontaneous hemopneumothorax. This internal accident is characterized by a sudden onset of unilateral chest pain which may or may not subside rapidly and is followed in a period of from hours to days by weakness, dyspnea and shock. The diagnosis is established by the blood count which demonstrates anemia, by the chest film which shows hydropneumothorax and by aspiration of blood from the affected side. The condition almost always occurs in males under forty and may show abdominal pain and rigidity as the presenting complaint. If the patient survives, he is usually not incapacitated if the affected lung is fully expanded and there is not too much residual pleural thickening.

Sixty cases of spontaneous hemopneumothorax have been reported. Even though 14 of these died and were autopsied, the etiology remains relatively obscure. Spontaneous hemopneumothorax may represent spontaneous pneumothorax with the unusual complication of hemorrhage. Both occur in young adults and come on spontaneously or in association with minor stresses causing increases in intrathoracic pressure. In half of the autopsies no hemorrhage source was found and the origin of the pneumothorax frequently unidentified. The hemorrhage has been explained on the basis of tears in the blood vessels of ruptured bullae and torn vascular pleural adhesions. During the production of interstitial emphysema, rupture of the vessels in the walls of alveolae may occur, the blood following the same pathway as the air into pleural cavity.

One case is reported who survived after treatment by repeated aspiration of the involved pleural cavity and multiple transfusions. —*D. Talley, M.D.*

CUGELL, DAVID W., and SCHERL, SIEGFRIED. Spontaneous pleural effusion in a newborn infant. *Am. J. Dis. Child.*, Oct., 1949, *78*, 569–572.

An unusual case of primary pleural effusion in a newborn infant is presented in this paper. In their review of the American literature, the authors found only 10 cases of primary pleural effusion in infants under one year of age. All cases were reported as spontaneous chylothorax. Their present case is the only known one of primary pleural effusion in a newborn infant which was nonchylous.

They state they can only speculate as to the causation of the effusion in their patient. Infection was not a factor, neither in the child nor was there any evidence of infection in the mother prior to delivery. Two remote possibilities are mentioned; traumatic pleurisy with effusion and concealed pneumothorax with effusion. With regard to the second possibility, they think the large effusion seen in the first roentgenogram could easily have concealed a small amount of air in the pleural cavity, especially when one realizes that the only initial film was taken with the patient in a horizontal position. Causes of spontaneous pneumothorax in the newborn have been listed by De Costa as follows: congenital anomalies such as pulmonary fistulas and abnormalities of pulmonary vessels; inflammatory processes associated with small pulmonary abscesses, from either pneumonia or septic emboli; trauma, including

fractured clavicle, fractured rib, direct parenchymatous injury and cough; mechanical obstructions such as mucus, vernix or meconium blocking the air passages, cord around the neck, struma or enlarged thymus; artificial respiration.—*R. S. Bromer, M.D.*

Judd, A. R. Allergy in pulmonary tuberculosis with special reference to autotuberculinization. *J. Thoracic Surg.*, June, 1949, *18*, 389–403.

Five cases of autotuberculinization are reported. All presented a characteristic syndrome and occurred following thoracoplasty or extrapleural pneumonolysis.

The onset of the condition is characterized by a high temperature elevation, which, however, is actively declining at the time the clinical symptoms and signs appear. Varying degrees of apprehension, blanchings of the skin, cyanosis, hyperpnea, dyspnea and general prostration are the outstanding symptoms noted. The Mantoux test is temporarily negative, and the roentgenogram shows an extensive "perifocal inflammation" around the foci of preexisting tuberculous implantations. In the more severe cases a mild delirium has been noted.

This reaction is due to a sudden collapse of a tuberculous lump which effects a sudden rise in the amount of tuberculin in the blood and lymph circulation. In consequence, there results a desensitization to tuberculin, i.e., autotuberculinization. During this period a marked increase in perifocal inflammation around all tuberculous foci may so alter the physiologic state of the individual that death may ensue.

Autotuberculinization presents a profound problem to the thoracic surgeon, for, at present, there appears to be no way by which this phenomenon can be predicted preoperatively. Two cases, not reported, died as a result of overwhelming reaction wherein not only the lungs themeslves but also the brain and meninges were involved.

The author presents an excellent discussion of allergy and immunity in tuberculosis. Numerous reproductions of roentgenograms illustrate the case reports.—*F. M. Reis, M.D.*

Ostrum, Herman W., and Serber, William. Early roentgen recognition of lower-lobe tuberculosis. *Radiology*, July, 1949, *53*, 42–48.

Lower lobe tuberculosis is more common than is generally appreciated.

The authors divide these cases into two types, those showing transverse streaks of infiltration in the perihilar region and those with more extensive involvement sometimes with cavity formation. Lesions which appear in the posteroanterior roentgenogram to be perihilar are often in lateral projection shown to be located distant from the hilus in the lower lobe. The lateral projection is essential in all cases where suggestive shadows are discerened in the perihilar region.

Other conditions giving similar roentgen appearance are (1) normal hilar markings, (2) bronchopneumonia and bronchiectasis, (3) nontuberculous lung abscess, (4) cancer.

Ten cases are reported, all in females. The authors state that this condition is more common in females.

In 6 of the 10 cases tubercle bacilli were found in the sputum. A seventh case was confirmed by autopsy. In the remaining 3 cases the subsequent history and roentgenograms were regarded by the authors as confirmatory of the diagnosis.—*Irving Schwartz, M.D.*

Ustvedt, Hans Jacob. Further investigations respecting bilateral hilar adenitis. *Acta med. Scandinav.*, May, 1949, *132*, 415–430.

Bilateral hilar adenitis, with or without E. nodosum at the same time, occurring in cases where we find no material for biopsy or characteristic affections of other organs, will not quite infrequently be due to tuberculosis, especially where the tuberculin reaction is strongly positive, but also where it is weak or negative. Boeck's sarcoid will far more seldom be present and only where the tuberculin reactions are weak or negative. A large number of the cases are characterized by joint affections, and we must reckon with the existence of a separate group which together with unilateral hilar adenitis, E. nodosum, E. multiforme and polyarthritis acuta may possibly bear relation to rheumatic fever.—*Charles Nice, M.D.*

Ravitch, M. M., and Hardy, J. B. Congenital cystic disease of the lung in infants and in children. *Arch. Surg.*, July, 1949, *59*, 1–36.

The authors review the literature concerning cystic disease of the lungs in the newborn and describe the various associated congenital malformations. Among the frequently associated abnormalities are anomalous lobar segments and anomalous vascular supply to the lungs, and especially to the anomalous lobes. There

have also been noted adenomatous growths of the mucus glands in some cases.

The authors state that it is their belief that these cysts of the lungs are congenital in origin and are derived from malformed bronchi and they point out the presence of the epithelium lining the cyst, which is bronchial in character, as well as the elastic tissue, smooth muscle, and cartilage in the walls of these cysts. The peripheral location of the cysts also suggests that the small peripheral bronchi have failed to establish communication with the air spaces.

They present 12 cases of their own varying in age from thirteen weeks to thirteen years. Of these 12 patients, there were 2 cases with associated anomalous lobes of the lung and in each case the anomalous lung was a trilobed left lung. One case had an anomalous arterial blood supply which was derived from the aorta, and a third had an anomalous systemic artery entering a cystic lower lobe of the right lung.

All of these patients, save one, was treated by surgical removal, of which 6 were single lobectomies, 4 were lobectomies of two adjacent lobes and 1 a pneumonectomy. There was 1 death among the cases, this being a child who died while awaiting operation. All cases presented some degree of infection at the time of operation.

At the time the patients presented themselves 3 had drainage tubes in the thorax, having been placed there elsewhere under the mistaken impression that the diagnosis was empyema. One of these patients had had a tube in place for as long as five years.—*Robert J. Reeves, M.D.*

STRODE, J. E. Cystic disease of the lung. *J. Thoracic Surg.*, June, 1949, *18*, 404–416.

Four cases of cystic lung disease are presented and the cases reported in the literature discussed.

The most practical classification of lung cyst is (1) bronchiogenic cysts, characterized by their walls being made up of elements of the bronchi and lined by cuboidal or columnar epithelium which may or may not be ciliated. These cysts may contain fluid, pus, blood or air alone or in combination; (2) alveolar cysts, which do not possess an epithelial lining but are lined by alveolar cells that are compressed together to form the wall. They always contain air.

Probably the vast majority of cystic lesions of the lung give rise to no symptoms and only some complicating factor draws attention to their presence. These may result from: (1) infection, (2) hemorrhage, (3) increase in size of cyst due to trapped air, (4) rupture of the cyst wall, resulting in simple or tension pneumothorax with or without empyema. All cysts or cyst-like structures are connected with a bronchus, but this communication with a bleb or bullous-like structure arising on the surface of the lung may be difficult or impossible to demonstrate.

The symptoms and differential diagnosis are discussed. Roentgen study is the most likely means of producing a diagnosis. Large solitary cysts frequently occur in very early childhood and are characterized by large areas of translucency and may or may not show fluid. They are frequently traversed by linear strands of trabeculation without any evidence of pulmonary markings. The picture often resembles that of pneumothorax. Many small cysts give a honeycomb appearance. The lesions are usually confined to one lobe or a segment of a lobe, and there is little or no inflammatory change in the adjacent lung or pleura. Bronchoscopy, artificial pneumothorax, introducing of iodized oil into the cyst and measuring of the intracystic pressure may help in establishing the diagnosis. Surgery is often the only means of differentiating between large infected solitary cysts and empyema. Treatment should be by surgery. The clinical entity of pulmonary cystic disease often remains unrecognized.

It should be suspected in the following situations: (1) dyspnea and cyanosis in early childhood or infancy in the absence of a cardiac lesion; (2) spontaneous pneumothorax or roentgen findings indicative of this condition; (3) hemoptysis in the absence of tubercle bacilli and with atypical roentgen findings; (4) patients in whom a diagnosis of empyema is made, particularly those who do not give a typical history of previous pneumonia; (5) an adequately drained lung abscess or empyema that does not respond well.—*F. M. Reis, M.D.*

SWAN, LAWRENCE L. Pulmonary adenomatosis of man; a review of the literature and a report of nine cases. *Arch. Path.*, June, 1949, *47*, 517–544.

The author has reviewed 900 pulmonary neoplasms from the Army Institute of Pathology and has selected 9 cases which fulfill the criteria

of adenomatosis. These criteria consist of (1) alveolar cellular proliferation of tall columnar mucus-producing cells; (2) absence of any intrinsic tumor at the bronchial tree; (3) absence of any primary malignant tumor in any other portion of the body.

This unique histopathological group of pulmonary neoplasms is the so-called alveolar cell tumor group. It is universally felt that the origin of this particular tumor is independent of the bronchi. It appears to rise in the alveoli of the lungs, and while having a histopathologically benign appearance, clinically they must be considered to be malignant, since they may produce death by local growth or by metastasis. The author suggests the term "pulmonary adenomatosis," which when found to be malignant should be further modified by the term "cancerous pulmonary adenomatosis." The author presents an excellent and exhaustive review of the literature, with full discussions of nomenclature, theories on etiology, histogenesis and comparative pathology. No roentgenograms are presented, but the gross and histopathological appearance of this unusual tumor is thoroughly described.—*C. L. Hinkel, M.D.*

Hengstmann, Hermann, and Wittekind, Dietrich. Zytologische Frühdiagnose des Bronchialkarzinoms mit Hilfe der gezielten Bronchialsonde. (Early cytological diagnosis of bronchogenic carcinoma by directed bronchial probing.) *Deutsche med. Wchnschr.*, Jan. 20, 1950, *75*, 101–104.

The paper reports a new method of obtaining bronchial secretion in cases suspected of bronchogenic carcinoma by probing the diseased bronchus under fluoroscopic control and examining the material obtained by aspiration with the usual cytological methods (Pappenheim's stain, Papanicolaou method, paraffin slides from larger particles).

After anesthesia of the upper air passages and the bronchial tree a rubber catheter, containing a ureter catheter with a mandrin, is introduced into the neighborhood of the lesion in the bronchus and after retraction of the ureter catheter and mandrin, aspiration with a 200 cc. syringe is carried out.

Twenty-one cases of clinically and roentgenologically suspicious bronchogenic carcinoma were examined by this method, 13 of these located in the upper lobe bronchi. In 19 cases a positive diagnosis of carcinoma was obtained. Examination of the sputum of these 21 cases was positive for carcinoma in 7 cases only, negative in 9 cases, 6 did not raise sputum.

The method seems to be of value in early cases, in lesions of the upper lobes, and peripheral lesions which cannot be visualized and biopsied by the bronchoscope and in cases where bronchoscopy is contraindicated.—*Karol E. Matzinger, M.D.*

Frey, E. K. Der Lungenkrebs. (Carcinoma of the lung.) *Deutsche med. Wchnschr.*, Jan. 6, 1950, *75*, 29–32.

Carcinoma of the lung is the second most common cause of cancer death in men and the most common one for those between forty-five and fifty-five, in a statistical study from five departments of pathology in Bavaria, 1945–1947, while it was fourth place in a study for the years 1925–1933.

This cannot be attributed only to the increased duration of life. A contributing factor though still controversial may be the inhalation of tobacco smoke, particularly from cigarettes. Radium emanation is known to cause cancer of the lung. In radium and uranium miners 60 to 70 per cent were found to have carcinoma of the lung on autopsy, 25 per cent of these had more than one primary tumor while practically no evidence of bronchogenic carcinoma was found in non-miners in the same area.

Epidermoid carcinoma was found most frequent with oatcell and undifferentiated carcinomas next and only 10 percent had adenocarcinomas.

Early diagnosis is imperative. Cough, expectoration, particularly when bloody, pain, repeated infection must be considered as significant particularly in men over forty.

Roentgen examination, bronchoscopy, cytological studies and in selected cases bronchography should establish the diagnosis. The author refers to Sauerbruch's description of narrowing of the bronchus or bronchial occlusion and filling defects as demonstrated in bronchograms as a characteristic sign of cancer.

The treatment of choice remains surgery, particularly pneumonectomy with lobectomy possible in selected cases. Nitrogen mustard and related agents as well as radiation treatment may be of palliative value, but cannot cure bronchogenic cancer.—*H. P. Mueller, M.D.*

ROENTGEN AND RADIUM THERAPY

Painter, Elizabeth E., and Brues, Austin M. The radiation syndrome. *New England J. Med.*, June 2, 1949, *240*, 871–876.

The authors critically review previous work and present knowledge of radiation effects, and the implications of data acquired. The radiation syndrome following a single total body LD_{50} dose of external or internal radiation begins, after a few hours latent period, as an initial shock period analogous to severe radiation sickness, with prostration, vomiting, and diarrhea. In some species, but not in man, there is a marked fall in blood pressure due partly to a circulating factor. The pathological physiology of radiation sickness is obscure. In therapy, antihistaminic drugs, epinephrine, and sodium chloride appear helpful, while liver extract, pentose nucleotides, vitamin B elements in the absence of deficiency, vitamin C, and adrenocortical extracts are not clearly restorative.

Recovery from initial shock is prompt, and subjects are clinically well for just over one week when an acute phase supervenes during which most fatalities occur. Even before the acute period clinically, the lymphocyte count has fallen abruptly, the granulocyte count fallen gradually, erythrocyte sedimentation rate increased, and clotting time prolonged. A complex but regular pattern of blood chemistry changes, mostly of obscure physiologic significance, appears. Diffuse hemorrhages throughout the skin and viscera are associated with a greatly increased blood heparin concentration. Protamine and toluidine blue, which inactivate heparin, return clotting time to normal and control hemorrhage. A general toxemia appears, partly due to tissue break-down products, and partly to the eleboration of bacterial toxins in the presence of leukopenia.

Subjects surviving thirty days fall into a subacute catagory characterized by fluctuating leukocyte count, severe anemia, progressive emaciation, and graying of dark-haired subjects. A later chronic phase is characterized by shortened life span and sporadic increase in certain tumors.

Nearly all physiologic systems are damaged by total body irradiation. Closely similar manifestations are seen after administration of the nitrogen mustards or urethane, in anaphylactic shock, agranulocytosis, and the "alarm reaction" of Selye. Direct damage to radiosensitive cells explain much of the picture, but further understanding of the syndrome is required for prevention and therapy.—*Henry P. Brean, M.D.*

Wood, Constance A. P. Some factors influencing response of cancer to radiation. *J.A.M.A.*, June 11, 1949, *140*, 513–520.

This paper deals with one aspect of the whole problem of radiobiology. Radiation therapy attempts to convert the viable cells in a carcinoma (resting and mitotic cells) into nonviable cells (differentiating and degenerating cells). These changes expressed in graph form, accurately foretell the clinical results in a majority of cases as compared with immediate microscopic effect.

Failure of radiation treatment is seen when the cells of the tumor lack the capacity of differentiating (becoming nonviable) or when there exists a precancerous lesion characterized by a relative increase of viable cells (resting and mitotic cells). Whereas the frank malignancy may respond to irradiation, the precancerous area will not and will subsequently give rise to a new tumor. One-third of the failures in therapy of cancer of the mouth and throat are due to the existence of precancerous lesions.

The author concludes that further improvements in radiotherapy are more likely to stem from the advancement of radiobiology than from improved physical technique.—*Gabriel Whiteman, M.D.*

Reinhard, E. H., Good, J. T., and Martin, E. Chemotherapy of malignant neoplastic diseases. *J.A.M.A.*, Feb. 11, 1950, *142*, 383–390.

During the last decade, potent carcinolytic compounds have been discovered which can be tolerated by animals and human beings in at least partially effective doses. Drugs which have aroused a great deal of interest include Serratia marcescens polysaccharide, KR (carcinolytic substance of Trypanosoma cruzi), antireticular cytotoxic serum (ACS), stilbamidine, and ethyl stibamine, folic acid conjugates, folic acid antagonists, urethane and the nitrogen mustards. At present, chemotherapy of cancer is at best palliative and retardation of tumor growth when it occurs at all is temporary. Some of the most experienced investigators in the field of cancer research doubt whether cure of cancer in this sense is within the realm of

possibility and certainly this goal is not apt to be achieved in the near future.

Stilbamidine and Ethyl Stibamine. Stilbamidine is known to be effective in the treatment of kala-azar, as both kala-azar and multiple myeloma are characterized by hyperglobulinemia. Snapper began treating multiple myeloma with this drug. The rationale for the use of stilbamidine is not clear as the drug acts directly on the parasite causing kala-azar and has no effect on the abnormal protein. Nevertheless, Snapper observed that, after administration of the drug, large basophilic inclusion bodies appear in the myeloma cells but not in any other cells in the bone marrow. In a pooled survey of 186 patients with multiple myeloma treated with this drug, 24.7 per cent experienced complete relief of pain and 38.7 per cent obtained partial relief of pain; the remainder of the patients were unimproved or became worse. Rubenstein treated patients having multiple myeloma with ethyl stibamine and observed relief of bone pain. The evidence at present is not convincing that either stilbamidine or ethyl stibamine is of great value in the treatment of multiple myeloma. There is no evidence that multiplication of the tumor cells is significantly retarded or that the duration of the disease is increased.

Urethane. Patterson and her associates in treating far advanced cases of malignant disease in humans with urethane noted that leukopenia frequently develops. This observation led to the trial of urethane in human leukemia. Satisfactory regression of the leukocytes in chronic myelogenous and chronic lymphatic leukemia has been obtained using urethane in 2 gram to 5 gram daily doses for two to six weeks or until the leukocyte count drops to 20,000. The data in the literature and the authors' experience do not suggest that urethane will supplant such forms of therapy as roentgen rays, P^{32} and nitrogen mustard.

Vitamins and Vitamin Deficiencies. Attempts to retard tumor growth by the production of biotin deficiency have been unsuccessful. Production of a pyridoxine deficiency apparently inhibits the growth of certain transplanted tumors in mice, but there is no evidence of a specific effect. Teropterin (pteroyltriglutamc acid—a folic acid conjugate), has been reported to improve the sense of well being, appetite and strength of patients and to relieve pain in a variety of malignant tumors, but there is no convincing evidence that either teropterin or diopterin produces significant effective improvement in any type of cancer. Teropterin cannot be regarded seriously as a chemotherapeutic agent against cancer.

Folic Acid Antagonists. Several years ago Farber, Heinle and Bethel observed that the administration of folic acid or its conjugates apparently intensified the severity of acute leukemia. It was natural, therefore, that when synthetic compounds which antagonize the physiologic activity of folic acid were prepared, their effect on acute leukemia should be studied. Farber summarized data on 60 children with acute leukemia treated for three weeks or longer with aminopterin, amethopterin (4—amino-methyl-pteroylglutamic acid) or amino-an-fol (4—amino-pteroylaspartic acid). Definite clinical and hematologic improvement occurred in somewhat more than 50 per cent of these patients. While spontaneous remissions may occur in up to 10 per cent of children with acute leukemia, the results obtained with folic acid antagonists are too pronounced to be attributed to incidental abatement. An occasional spectacular remission may occur, but the fact remains that most remissions produced by the folic acid antagonists are incomplete and of brief duration. Most investigators using folic acid antagonist therapy have observed more frequent remissions of acute leukemia in infants and children than in adults. The severe toxic reactions produced by these drugs include stomatitis, ulceration of the mucous membranes of the mouth, diarrhea, gastrointestinal hemorrhage, leukopenia, thrombopenia and aplasia of the bone marrow. Sometimes, these changes appear after relatively small doses. In spite of the severe toxicity of these drugs the evidence is convincing that temporary remissions of acute leukemia occur in a significant percentage of patients receiving such therapy.

Nitrogen Mustard. During World War I, considerable work was done on the toxicology of mustard gas. Systemic effects on the bone marrow with resultant leukopenia were recognized. With the onset of World War II intensive study of mustard gas and related compounds was resumed. Most of the clinical work on the treatment of neoplasm had involved the use of methyl bis (2—chloroethyl) amine hydrochloride, known as nitrogen mustard. These compounds exert a specific nucleotoxic action by interfering with chromosomal mechanisms and mitotic division in a manner somewhat analogous to the effects of roentgen rays. The

susceptibility of cells to the lethal effect of the mustard is related to the rate of cellular multiplication. Nitrogen mustard produces cellular fragmentation in lymph nodes within ten hours, followed later by lymphatic atrophy. In the bone marrow, early changes include altered staining reaction of the hemopoietic cells followed by progressive aplasia. In the intestines early vacuolization and nuclear swelling of the epithelial cells lead eventually to necrosis and desquamation with hemorrhage. More than seventy articles have been published on the clinical uses of nitrogen mustard. Gelhorn and Jones have reviewed this literature and have found that favorable responses to nitrogen mustard therapy have been reported in Hodgkin's disease, lymphosarcoma, giant follicular lymphoma, chronic lymphocytic leukemia, chronic myelocytic leukemia, polycythemia vera, rhabdomyosarcoma, mycosis fungoides and anaplastic cancer of lungs. Equivocal responses have been reported in lymphoepithelioma, Boeck's sarcoid, disseminated lupus erythematosus, neuroblastoma and Ewing's tumor. No response has been observed in acute leukemia, aleukemic leukemia, central nervous system tumors, squamous cell carcinoma of the lungs, carcinoma of the genitourinary or gastrointestinal tract and oral cavity, carcinoma of the breast, melanosarcoma, fibrosarcoma, Kaposi sarcoma, osteogenic sarcoma and reticulum cell sarcoma. The authors believe that nitrogen mustard is of definitely proved value only in Hodgkin's disease and to a lesser extent in lymphosarcoma. Evidence is not convincing that nitrogen mustard is superior to roentgen radiation or other forms of therapy for other conditions in ordinary circumstances. Nitrogen mustard may be the treatment of choice when anaplastic tumor is producing pressure on a vital organ because it does not produce edema in tumor tissues such as is common after irradiation. Nitrogen mustard has the following disadvantages: (1) it cannot be applied locally; (2) profound depression of bone marrow function is common even with therapeutic doses; (3) it is generally agreed that remissions are shorter than those induced with roentgen irradiation. Because of these disadvantages, it is now generally agreed that roentgen therapy is the treatment of choice for localized Hodgkin's disease with minimal or no systemic manifestations. Treatment with nitrogen mustard should be considered (1) when the patient has been given an adequate course of roentgen irradiation without response because repeated roentgen courses in the past have rendered the lesions "roentgen-fast," (2) when trophic skin changes preclude the further use of roentgen therapy, and (3) in those cases of Hodgkin's disease characterized by high fever, sweats, malaise, generalized aching pains, anorexia, weight loss, and pleuritis, unaccompanied by pronounced localized enlargement of lymphnodes, splenomegaly or hepatomegaly.—*S. G. Henderson, M.D.*

BUTENANDT, ADOLF. Zur physiologischen Bedeutung des Follikelhormons und der östrogenen Wirkstoffe für die Genese des Brustdrüsenkrebses und die Therapie des Prostata-Karzinoms. (On the physiological importance of the follicular hormone and the estrogens in the genesis of mammary carcinoma and the therapy of prostatic carcinoma.) *Deutsche med. Wchnschr.*, Jan. 6, 1950, *75*, 5–7.

Carcinogenic materials may be divided into "absolute" and "accessory" carcinogens, the former independent of the genetic nature of the experimental material and producing tumors at the site of application or in certain special organs, and the latter merely increasing the tumor incidence in cancer strains.

Butenandt *et al.* (1943, 1949) demonstrated increased systemic and no local incidence of tumors in a cancer strain of mice following injection or painting with a lipoid free, unsaponifiable extract of human liver.

Kaufmann *et al.* (1949) increased the incidence of mammary carcinoma in the same strain from 46 per cent to 83 per cent by painting with benzene.

Law obtained an increased incidence of pulmonary tumors in a suitable strain by the injection of desoxycholic acid.

Accessory carcinogens are much less specific than absolute carcinogens and are probably more significant in human cancer than are the absolute carcinogens in the so-called occupational cancers.

Among the accessory carcinogens, proliferation producing hormones (follicular hormones or synthetic estrogens for the breast, testosterone for the prostate, thyrotropic and adrenocorticotropic hormones) have specific organotropic effects.

That the follicular hormone is not an absolute, but an accessory carcinogen, is demonstrated by the following facts:

1. Non-tumor-bearing strains of mice are unaffected by massive doses.

2. Tumor-bearing strains develop mammary carcinomas only in the female at a definite rate (spontaneously).

3. Castrated females do not develop mammary carcinoma (spontaneously).

4. Hormone administration, in sufficient quantity, to males or castrated females produces a tumor rate similar to that in normal females of the strain.

The author and his associates (1949) experimented with natural and synthetic estrogens in 5,770 mice and found that:

1. Massive, unphysiological doses resulted in earlier appearance and higher total incidence of mammary carcinomas, incidence being similar in males and females.

2. The degree of the effect, with adequate dosage, seemed more closely related to the strain than to variations in dosage.

3. There was no difference in the effects of natural or synthetic estrogens when given in comparable doses.

The mechanism of the earlier appearance and increased total incidence is earlier development and marked hyperplasia of the breast, resulting in an absolute increase in the number of cells from which a cancer might originate.

The use of estrogens as physiological opponents of testosterone in the treatment of prostatic carcinoma brings about the possibility of an increase in the incidence of carcinoma of the male breast. Liebegott, in 1948, described the first case, and others have been noted in the United States. Thus the results obtained in experiments with mice are seen to apply to man. In the estrogenic therapy of prostatic carcinoma it is suggested that there be careful checking of the breasts, with early mastectomy, if needed, and that the dosage of estrogens be kept as low as possible.

In conclusion, the author states that the follicular hormone is only one of three factors necessary for the development of breast cancer, the others being the proper genetic background and the Bittner milk factor.—*J. J. B. Light, M.D.*

Peirce, C. B., Cone, W. V., Bouchard, J., and Lewis, R. C. Medulloblastoma; nonoperative management with roentgen therapy after aspiration biopsy. *Radiology*, May, 1949, *52*, 621–632.

The authors believe that roentgen therapy without major surgical intervention is the treatment of choice for medulloblastoma. They contend that biopsy diagnosis is preferable to differentiation by irradiation response, because there will be a gain of at least ten days in selection of lesions suitable for early surgical treatment.

A technique for twist-drill aspiration biopsy of suspected cerebellar lesions is described. The procedure is simple and safe but should be done only after careful clinical and ventriculographic examinations have definitely placed the tumor in the posterior fossa.

They strive to deliver a tumor dose of at least 4,500 r to the primary lesion, in four weeks using three or four ports, 200 kv., and Thoraeus filter. In the following two weeks 2,000 r, measured in air, is delivered to the spinal canal.

This is a preliminary report on 5 patients. The immediate results are impressive. One patient had two additional, similar irradiation courses because of early signs of tumor recurrence, and is well thirty-seven months after initial treatment. Two are well twenty-two and nineteen months without recurrence. One was well for six months but died due to an automobile accident. One died after nine months.—*Arthur A. Brewer, M. D.*

Scharnagel, Isabel M., and Pack, George T. Multiple basal cell epitheliomas in a five year old child. *Am. J. Dis. Child.*, May, 1949, *77*, 647–651.

The occurrence of several hundred basal cell epitheliomas in a five year old child is a sufficient rarity, the authors believe, to justify publication. It has been their experience that squamous cell carcinomas occur more frequently in young subjects than do the basal cell type. The lesions in the case reported were multiple basal cell epitheliomas of the hair matrix type. They were so numerous that they could not be counted, but more than 1,000 multicentric foci of basal cell lesions were present in the child. Many dark raised spots first appeared on the anterior chest wall and later spread to the axillas and back. Shortly after birth, the infant had experienced obvious difficulty with breathing. A diagnosis of enlarged thymus was made at that time and the patient received four roentgen treatments. The skin over the portal of treatment became red and subsequently persistent brownish tan. Innumerable macular and, later, papular spots had spread to involve not only

the skin which was irradiated but also the skin of the back and axillary regions. A roentgenogram of the chest showed essentially normal findings relative to the lungs, another of the skull showed considerable enlargement as in hydrocephalus.

The patient was admitted four times to the hospital and four segmental excisions were made during the first three stays. At the last scattered lesions were electrodesiccated. All operations were done under general anesthesia. Extensive roentgenographic, electrocardiographic and chemical studies were made to determine whether any fibrotic changes in the heart and lungs had occurred but none could be found.—*R. S. Bromer, M.D.*

KLOSTERMYER, L. L. and BURGESON, PAUL A. Radiation therapy of the Guillain-Barré syndrome. *Radiology*, July, 1949, *53*, 85–87.

The Guillain-Barré syndrome is an obscure condition, the etiology is unknown, and therapy has been generally unsatisfactory. It has been called infectious polyneuritis, acute infective polyneuritis, acute ascending paralysis, and infectious neuronitis.

One important finding is that of a high protein spinal fluid level with a normal cerebrospinal fluid cell count. The authors give a good general discussion of the disease, showing different types together with a discussion as to its possible etiology.

Based on the relief of pain by roentgen irradiation, the authors treated 2 cases, one of the acute type and one of the chronic type. The cases are reported in detail, and the results in these 2 cases are spectacular, justifying their plea for further trial therapy in this condition. —*Allan Tuggle, M.D.*

COGAN, DAVID G. Lesions of the eye from radiant energy. *J.A.M.A.*, Jan. 21, 1950, *142*, 145–151.

Electromagnetic radiation of various wavelengths (and the comparable corpuscular radiation) is discussed in relation to ocular lesions from three standpoints: the common sources of the various types of radiation which have caused ocular lesions; the transmission and absorption of radiant energy in the ocular media; and the clinical characteristics of the ocular lesions caused by the various types of radiant energy. An excellent figure summarizes the article.

Radio and diathermy waves (and direct current) penetrate the eye, the usual lesion produced is cataract. Infra-red rays are largely absorbed in the anterior portion of the eye, but the shorter infra-red rays come to a focus behind the retina; the common harmful results are cataract and scotoma. Visible rays are absorbed superficially except for the transparent media; their harmful effect is scotoma. Ultraviolet and grenz rays (and beta or cathode rays) are absorbed in the anterior portions of the eye; the lesion produced is keratoconjunctivitis. Roentgen rays and gamma rays (and neutrons) are transmitted through all media of the eye; their usual harmful effects are keratoconjunctivitis and cataract. Cosmic rays are also transmitted through all the media, but produce no harmful effect so far as is known.

"With the type of roentgen rays usually employed in roentgen therapy (100 to 200 kilovolts), the minimal cataractogenic dose is of the order of 500 to 800 r."

"Radiation burns of the eye are either permanent or spontaneously reversible. There is no specific form of therapy for any of them. . . . The only adequate form of treatment for radiation lesions of the eye is prophylaxis." —*H. G. Moehring, M.D.*

SMITH, MARCUS J., and STENSTROM, K. WILHELM. Parotid tumors; review of ninety-three cases. *Radiology*, May, 1949, *52*, 655–661.

In an attempt to obtain some information concerning the results of treatment of parotid tumors, the authors have reviewed the records of 93 cases of such tumors referred to the radiation therapy section of the University of Minnesota Hospitals between 1927 and 1947. Although treatment is primarily a surgical problem, irradiation may be required either in conjunction with surgery or in a given case as the only suitable method.

Mixed tumors of the parotid probably arise from epithelium of salivary or mucous gland or from detached salivary gland anlage. There has been considerable controversy as to whether they are benign or malignant. The present evidence suggests that mixed tumors should not be considered unqualifiedly as benign tumors, but rather should be thought of as potentially, if not actually malignant. In the authors cases mixed tumors constituted 63 per cent of the series. The age range was from thirteen to seventy-two years, the average being 39.7 years at the time of treatment. Characteris-

tically, growth was very slow and there was no pain, although mild aching was occasionally present. The non-tender mass was attached to the gland but not to the skin. The original treatment was by surgery, roentgen rays and radium. In this series in patients with a ten to twenty-year follow-up there was a 30 per cent recurrence rate. The recurrences were all retreated with radiation therapy and 5 out of 7 were free from symptoms at the last examination, indicating the value of radiation therapy.

Carcinoma of the parotid gland accounted for 37 per cent of the series. The average age of these patients was 63.3 years. Clinically there were tender, hard, rapidly enlarging masses in the parotid region showing marked local invasive tendencies. Often the masses were ulcerated and fungating, and severe pain was frequent. Seventh nerve involvement and fifth nerve neuralgia were not uncommon. Many of these tumors had been present for years before they had commenced to enlarge rapidly, one for thirty-eight years. Treatment was by more radical surgery than for mixed tumors and more postoperative irradiation was administered. Inoperable cases were treated by irradiation alone and fair to good palliation was obtained. In spite of surgery and postoperative irradiation the five year survival rate was only 27 per cent.

Poor results can probably be correlated with the failure of the patient to report for early treatment. They can be blamed partially on a widespread belief that haste in the treatment of mixed tumors is not necessary. Since biopsies are taboo in mixed tumors and since it is often difficult to distinguish between a mixed tumor and a carcinoma, it seems advisable to urge operative removal, subsequent irradiation and microscopic study as soon as possible after detection of the tumor in order to avoid the poor results obtained in the treatment of carcinomatous parotid tumors that have been dormant for many years. Perhaps preoperative irradiation should be added to this armamentarium.—*Arthur E. Childe, M.D.*

Gibbel, Melvin I., Cross, James H., and Ariel, Irving M. Cancer of the tongue; a review of 330 cases. *Cancer*, May, 1949, *2*, 411–423.

The authors review 330 cases of primary tongue cancer treated by various methods at the Veterans Hospital at Hines, Illinois, over a fifteen year period and comprising 28.3 per cent of all intraoral cancers seen, or 1.8 per cent of all cancer cases admitted. The average age was 52.6 years. Twenty-two per cent showed positive serological findings against only 5 per cent for the over-all hospital admissions. Leukoplakia was noted in 10 per cent of all tongue cases and 22 per cent of luetic patients.

Cancer was most frequently encountered in the base of the tongue (47.8 per cent). It was never seen in the dorsum immediately in front of the lingual V. In 95.7 per cent the lesion was histopathologically squamous cell carcinoma; in 4.3 per cent transitional cell carcinoma was found. On admission 68.8 per cent of cases showed cervical metastases.

Treatment of cases without metastases consisted of external or peroral roentgen therapy in doses of 6,000–8,000 r, supplemented by interstitial radon seed implantation of 4 to 7 erythema doses. Partial glonectomy was sometimes added. Patients with cervical metastases were treated by radical surgery combining resection of part of the tongue, floor of the mouth, and contiguous pharyngeal structures with a hemimandibulectomy and radical neck dissection. The five year cure rate for the series was 14.2 per cent.—*J. A. Campbell, M.D.*

Wolfe, John J., and Platt, William R. Postirradiation osteogenic sarcoma of the nasal bone. *Cancer*, May, 1949, *2*, 438–446.

The authors find 60 cases of osteogenic sarcoma reported in the literature probably attributed to the cause-effect relationship of roentgen and radium therapy, and add 2 additional case reports of sarcoma involving the nasal bones. Both cases were irradiated for low grade skin cancer and showed no subsequent infection of osseous tissue. The first case received approximately 330 mg. hr. of radium and 1,031 roentgens of roentgen radiation between 1921 and 1943. The total radiation received by the second case was not determined. Resection and plastic repair controlled one case and the other showed roentgenographic evidence of continued destruction.—*J. A. Campbell, M.D.*

Hoboek, Andreas. Dental prostheses and intraoral epidermoid carcinoma. *Acta radiol.*, 1949, *32*, 259–275.

Five hundred and sixty intraoral epidermoid carcinomas were treated at the Norwegian Radium Hospital between the years 1932 and 1945. By study of this tumor material it has

been possible to demonstrate a causal connection between irritation caused by prostheses and the development of cancer in 86 of the cases. Sixty, or 70 per cent, of the cancers were in women and of these 12, or 20 per cent, had a marked Plummer-Vinson syndrome.

The author emphasizes the importance of atrophy of the mucous membranes as seen in sideropenic anemia (Plummer-Vinson syndrome) and senile atrophy in the production of precancerous states. He points out that atrophy of the mucous membranes together with chafing of prostheses may result in cancer of the mouth. A connection between the presence of leukoplakia and cancer and also between stomatitis of the palate and carcinoma in this region is shown.—*Mary Frances Vastine, M.D.*

KAAE, S., and GLAHN, M. Case of sarcoma in irradiated mandible. *Acta radiol.*, June 30, 1949, *31*, 431–434.

Sarcoma arising as a sequela of irradiation of bone is an uncommon condition. Seventeen cases have been gathered from medical writings, 11 cases have been seen at the Memorial Hospital, New York, and there are Martland's 10 cases in radium dial painters.

The initial lesions treated by roentgen rays or radium were (1) tuberculosis, (2) benign giant cell tumors, (3) bone cysts, and (4) other benign diseases. Two cases were irradiated postoperatively for carcinoma of the breast. The roentgen doses were large. In 9 of the cases reported by Cahan *et al.* the depth doses in the bones were calculated to be over 3,000 r.

Wood and Coley found that bone doses larger than 3,000 r usually caused permanent damage to the regenerative capacity of normal bone. Doses of more than 5,000 r were likely to cause complete devitalization of adult bone but the bones of children survived much larger doses. Cahan *et al.* suggest that the development of osteogenic sarcoma in irradiated bone is analogous to the development of leukemia in marrow or epithelioma in the skin that has undergone severe atrophy from irradiation.

The latent period, calculated from the date of the last roentgen or radium treatment prior to the onset of the clinically determinable sarcomatous change, was three to twenty-two years. In most cases the sarcomas were located in the long bones. In only one case was the mandible involved.

The most prominent symptom was a rather sudden onset of steady and progressively increasing pain in the area. It is emphasized that when a patient returns with complaints of pain with or without swelling in an area which had been irradiated four or more years previously, malignant change should be suspected.

The authors report a case of fibrosarcoma in the mandible of a sixty-two year old male who had been treated with radium for a carcinoma in the same place thirteen years previously.—*Mary Frances Vastine, M.D.*

CUTLER, M. H., MARCUS, RICHARD E., and LEDERER, FRANCIS L. Evaluation of the effects of radiation on non-malignant lesions of the nasopharynx. *Radiology*, June, 1949, *52*, 816–818.

The authors present a series of 50 patients with lymphoid hypertrophy and hyperplasia in the nasopharynx treated with radiation according to the method of Crowe, in an attempt to evaluate the method.

By means of a nasal applicator, the end of which contained a specified amount of radioactive material, the authors treated 50 cases which were divided into four groups with the following results:

Group I: Thirteen cases of well defined or fixed deafness were treated with negligible results.

Group II: This group consisted of 25 cases, 23 children and 2 young adults, whose outstanding symptoms were allergic, who had an allergic family background, and who had lymphoid masses of significant size in the nasopharynx. All had had tonsils and adenoids removed. The results here were almost all favorable over the period of two to four months that they were observed.

Group III: Seven adults and 1 child with intermittent symptoms of "stopping up" in the ears, tinnitus and "clicking" noises in the ears were treated. One-half of these reported some improvement after irradiation.

Group IV: Three patients with chronic aural discharge who were treated in the hope of relieving eustachian tube obstruction and thus restoring normal physiology, received no benefit.—*John F. Gibbons, M.D.*

SIMMONS, MARVIN W., and ARIEL, IRVING M. Carcinoma of the nasopharynx; report of 150 cases. *Surg., Gynec. & Obst.*, June, 1949, *88*, 763–775.

Malignant lesions of the nasopharynx are

much more common than statistics reveal because of the frequency of misdiagnosis. The nasopharynx is difficult to examine and the symptoms falsely indicate that the origin of the disease entity is located elsewhere. In the series presented in this paper, 150 consecutive, unselected cases from Hines Veterans Administration Hospital were reviewed and studied. In each patient biopsy from the nasopharynx was positive. All the patients were males with an average age of forty-five years. Most common site of origin was Rosenmueller's fossa in 26 cases (17.7 per cent) of the 150 patients. Of the 150 cases there were 128 deaths with 37 postmortem examinations. Extension intracranially was demonstrated in 9 (24 per cent) of the autopsies and metastases below the level of the clavicle occurred in 20 instances (54 per cent). A characteristic of the disease is early cervical metastases which were found in 125 patients upon admission (83.3 per cent). Only 20 patients (13.3 per cent) failed to demonstrate cervical metastases during the course of the disease.

Neck swelling was the most common initial symptom occurring in 79 patients (52.7 per cent). Next was pain on the side of the face and head which occurred in 25 patients (16.6 per cent). Rarely did initial symptoms referable to the nasopharynx occur.

Cranial nerve findings were seen in 44 patients (29.3 per cent) upon admission. The sixth nerve was involved most often. A total of 55 patients (36.6 per cent) had cranial nerve paralysis sometime during the course of the disease. Horner's syndrome was observed in 26 instances (17.3 per cent).

The patient waited an average of 3.2 months after symptoms began before visiting a doctor. An average of 6.9 months elapsed before the physician made the correct diagnosis. A period of 10.1 months elapsed in the average case after a significant symptom commenced before adequate therapy was instituted. In the 128 patients that succumbed an average time interval of twenty-seven months occurred from the date of onset of symptoms to death. With adequate treatment, the time interval averaged thirty-one months from onset of symptoms to death. When no irradiation was administered the patients lived an average of seventeen months. With treatment of the metastases alone because of the erroneous diagnoses or for palliation, an average time of twenty-one months was found from symptoms to death.

Prior to admission to the hospital the correct diagnosis was made by referring physicians in only 58 instances (38.7 per cent). Of the 78 determinate cases only 7 remained free of the disease for five or more years. The net five year survival rate was 9.8 per cent. All the cures occurred in patients who had developed cervical metastases. No cures were obtained in cases with intracranial extension. The treatment is exclusively radiological.—*Mary Frances Vastine, M.D.*

Baclesse, François. Roentgentherapy in cancer of the hypopharynx. *J.A.M.A.*, June 11, 1949, *140*, 525–530.

Cancer of the hypopharynx has a poor prognosis, because tumors occurring in this site are usually of an ulcerating and destructive nature. These lesions are difficult to cure because of complications such as infection, involvement of the cartilage, and sometimes considerable extension to the surrounding structures.

The author classifies the hypopharynx into the upper or membranous part and the lower or osteocartilaginous part. Those patients surviving malignancies of the hypopharynx are for the most part those in whom the cancer originated and developed in the upper part.

In early cases the diagnosis is easy, but in advanced cases, laryngoscopic examination is the only way to determine the origin of the disease. The author stresses the importance of anteroposterior and lateral roentgenograms of the neck as an aid in the diagnosis of tumor.

The author reports 425 cases that have been studied and reported, of which 6 per cent were living and apparently healed after five years. These patients were treated with rather high doses (total skin dose distributed over two fields was 7,000, 7,500, 8,800 and 9,100 roentgens). The technique is reported in detail. The author states that he now attempts to reduce cutaneous reaction by prolonging treatment time and by reducing the size of the fields while increasing the total dose. Lymph node metastases are considered and in a great number of recent cases, lymph nodes, even though large ones, have, in some cases, seemed more amenable to treatment, at least temporarily, than the primary tumor.

Five year results on cancer of the oropharynx and nasopharynx are reported.

Numerous charts and diagrams accompany the article.—*Edsel S. Reed, M.D.*

Cunning, Daniel S. Diagnosis and treatment of laryngeal tumors. *J.A.M.A.*, Jan. 14, 1950, *142*, 73–77.

The symptoms of any lesion of the larynx vary from hoarseness, the most common, to dyspnea and croupy tendencies depending upon the amount and location of the involvement of the laryngeal structures. Pain is rarely experienced.

In the diagnosis of laryngeal lesions a complete and thorough examination of the larynx is all important wherein all parts of the larynx are clearly brought into view and adequately studied at time of the examination. It is highly important that the anterior commissure be adequately studied inasmuch as many malignant growths start in this area. Conduct of the examination of the larynx is discussed.

Laryngeal polyps, papillomata, vocal nodules, cysts, contact ulcer and cancer of the larynx are discussed. These conditions are treated from the standpoint of symptoms, gross appearance and usual management.

Cancer of the larynx is the most important of all tumors of the larynx.

The end results of five year cures with roentgen therapy of early cordal cancer are on a par with those of laryngofissure. The method of treatment with roentgen therapy is administration of 6,500 r to 8,000 r to the larynx in thirty to forty days, using small fields. (Other technical factors not given.)

Indications for the choice of therapeutic modality in cancer of the larynx are discussed as well as indications for combination of surgical procedure and roentgen therapy and close cooperation between the laryngologist and the radiation therapist is important at all times.

The article closes with discussion of some cases in detail and abstract of discussion at time of presentation of paper.

One chart is included listing tumors of the larynx and their pathologic distribution seen in the clinic of the Manhattan Eye, Ear and Throat Hospital between the years of 1944 and 1949.—*J. H. Gilmore, M.D.*

Pendergrass, Eugene P., and Kirsh, David. On the occurrence of herpes zoster in carcinoma of the breast. *Am. J. M. Sc.*, June, 1949, *217*, 674–680.

It is common knowledge among oncologists and radiotherapists that the incidence of herpes zoster in Hodgkin's disease, leukemia and metastatic carcinoma is greater than in the population at large, although statistics on the subject are not available. On the basis of large surveys, herpes zoster occurs in the proportion of 1 to 2 per cent of all diseases of the skin. The observance of 16 cases of this disease entity in a survey of 406 cases of carcinoma of the breast, giving an incidence of 4 per cent, prompted this clinical presentation.

Herpes zoster is generally conveniently classified into two groups. The idiopathic or primary and the symptomatic or secondary forms. The idiopathic herpes occurs in otherwise normal individuals, and characteristically produces a vesicular eruption which follows a zonal or segmental distribution and is accompanied by fever, leukocytosis and marked pain. The present-day conception of the disease regards a filtrable virus as the causative agent.

Secondary or symptomatic herpes has an obscure and mixed etiologic background, having been observed during and following a variety of disease entities. In addition, it has followed trauma, pressure from a spinal cord tumor, intoxication by poisons, and various neoplastic diseases.

Symptomatic herpes zoster is seen in fairly frequent association with Hodgkin's disease. Pancoast and Pendergrass in 1924 reported 4 cases of herpetiform eruptions in Hodgkin's disease and 1 case in ovarian carcinoma. They thought that herpes zoster occurred much more frequently in malignant conditions than was generally believed.

The existence of a symptomatic type of herpes zoster brought on by tumor metastases is denied by some investigators.

The records of 406 cases of carcinoma of the breast seen by the authors at the University of Pennsylvania Hospital from 1932 to 1939 were investigated to complete previous studies on this subject. Sixteen cases of herpes zoster were encountered, in 12 of whom there was evidence of metastatic disease either before or after the appearance of the cutaneous disease. The remaining 4 patients survived between six and twelve years after the herpetic attack with no evidence of metastatic malignancy.

Fourteen of the patients with herpes zoster received preoperative or postoperative irradiation with roentgen rays or both, only 2 receiving no irradiation. All 4 of the patients developing herpes without metastatic disease were subjected to irradiation.

In view of the multiplicity of inciting agents, the possible etiologic role of irradiation must also be considered. Twelve of the cases of herpes developed evidence of metastatic disease either before or after the appearance of the eruption. Of 350 cases operated upon, 218 (62 per cent) subsequently showed evidence of recurrent or metastatic disease. Thus, the incidence of herpes zoster in metastatic disease was 11 cases in 218 (5.0 per cent) while the incidence in those cases not showing metastatic disease was 4 cases in 132 (3.0 per cent).

Past evidence indicates that the metastatic disease merely prepares the soil for the invasion of the virus or causative agent of herpes zoster, rather than actually causing the disease itself. In some cases, knowledge of the association of herpes zoster and malignancy may aid in the uncovering of an otherwise cryptic neoplasm or unsuspected leukemia, although diagnosis rarely is a problem in breast carcinoma. All patients with herpes zoster should be subjected to a careful clinical study for possible neoplastic disease.—*Julian I. Gilliam, M.D.*

Moore, O. S., and Foote, F. W. The relative favorable prognosis of medullary carcinoma of the breast. *Cancer*, July, 1949, *2*, 635–641.

As defined by the Memorial Hospital in New York "medullary carcinoma" has a prognostic implication, especially when there is an associated lymphoid infiltration. Grossly the tumors are soft and anatomically circumscribed. They are more expansile than infiltrative.

One thousand consecutive cases of breast cancer were studied. Of these, 52 fulfilled the criteria for medullary carcinoma. Analysis of the five year end result of these cases reveals 82.7 per cent free of cancer; 17.3 per cent are dead; 11.5 per cent from cancer and 5.8 per cent from other causes. Thus, patients with medullary cancer of the breast have a five times better chance of five year survival after radical mastectomy than those with the more usual types.—*J. G. Lorman, M.D.*

Krebs, Carl, Nielsen, Howard, and Andresen, Poul E. Rotation treatment of cancer of the esophagus. *Acta. radiol.*, 1949, *32*, 304–316.

The authors report the results of rotation therapy in 217 cases of cancer of the esophagus and cardia. While the palliative effect has been excellent the curative effect has not been remarkable. Nevertheless, the average duration of life has been almost doubled by this therapy. In approximately 20 per cent of the patients the tumor was destroyed locally so that no remnants were demonstrable on the histopathologic specimens. However, only a few patients were cured, the rest dying of distant metastases. The authors believe that the salvage rate would be materially bettered if the patients could receive treatment early in the course of their disease. "By shortening the pre-treatment period we have a well founded hope of being able to obtain far better results."—*Mary Frances Vastine, M.D.*

Ariel, I. M., Head, J. R., Langston, H. T., and Avery, E. E. The use of interstitial radon seeds and needles in inoperable lung cancer. *Cancer*, July, 1949, *2*, 581–586.

The authors present a series of 17 cases of bronchogenic carcinoma found to be inoperable at exploratory thoracotomy and in which radon seeds and needles were implanted. An attempt was made to provide from 6 to 10 T.E.D. to all parts of the neoplasm. All patients received prompt but transient palliation (one to ten months). In one patient there occurred a reactivation of an old tuberculosis in the opposite lung. Another patient developed severe hemoptysis seven months following the insertion of radon. Sixteen patients succumbed on an average of 5.6 months following treatment.—*J. G. Lorman, M.D.*

Jacobs, Arthur, Riches, E. W., and Millen, J. L. E. Carcinoma of the bladder. *Brit. J. Radiol.*, July, 1949, *22*, 393–398.

Bladder tumors with a narrow pedicle and which can be easily elevated are best treated by diathermy. The solitary, sessile, broad based, papillary carcinomas and flat nodular infiltrating lesions are best treated by irradiation if the lesions are in the lower part of the bladder. The lesion is exposed through a cystotomy, and radium needles screened with 0.5 mm. platinum are used for 160 hours to give a total dose of 7,000 roentgens. The needles are arranged to produce homogeneous irradiation to an area including the tumor and a zone 1 cm. in diameter at its periphery. The arrangement is according to the system of Paterson and Parker. When small tumors are treated radon can be used.

The reaction to the irradiation may be severe and may last as long as a year.

Of 110 patients treated in a period of fourteen years, 11 were postoperative deaths, and 10 died of other causes; 37 lived five years or longer.

When partial cystectomy can be done, the five year survival rate is about 20 per cent.—*E. F. Lang, M.D.*

RICHES, E. W. Carcinoma of the bladder. II. Some further aspects of treatment. *Brit. J. Radiol.*, July, 1949, *22*, 398–402.

The author treats about one-third of his patients with carcinoma of the bladder with partial cystectomy and another quarter with total cystectomy. When the lesion is in a mobile part of the bladder and the lesion is accessible, partial cystectomy is the operation of choice. The five year survival rate is about 21 per cent. For palliation the author advises even ureteric transplantation. Roentgen therapy is also very useful in these cases.—*E. F. Lang, M.D.*

MILLER, J. L. E. Carcinoma of the bladder. III. Treatment by radon seed implantation and deep x-ray therapy. *Brit. J. Radiol.*, July, 1949, *22*, 402–405.

All lesions 7 cm. in diameter, or less, which can be made 1 cm. or less in thickness at operation, are treated with radon by the author. The tumor is visualized through a suprapubic systotomy and the superficial portion of the tumor removed by diathermy. The radon needles are placed according to the system of Paterson and Parker. When the lesion is beyond the scope of radon, but when it is still possibly curable, radical roentgen therapy is given, administering 6,000 roentgens to the tumor over a period of five weeks through six fields. The decision for either radon or roentgen therapy should be made at cystoscopy, because after a cystotomy roentgen therapy cannot so successfully be administered.

Out of 249 patients treated by radiotherapy in ten years, 54 survived five years. Of 168 patients treated with radon or with radical roentgen therapy in an attempt to cure the patient, the survival rate was 28 per cent for five years.—*E. F. Lang, M.D.*

FERNANDEZ-COLMIERO, J-M. Le cancer primitif de l'utérus après la guérison par radiothérapie d'un autre cancer du même organe. (Primary cancer of the uterus following the healing of a previous carcinoma of the same organ treated by radiotherapy.) *Presse méd.*, June 15, 1949, *39*, 565–566.

The 2 cases reported are from the Fondation Curie, Paris. The author has previously pointed out (1946) that what is sometimes considered a recurrence of carcinoma is in fact a new primary carcinoma; and the 2 cases here reported with totally different histopathological structure of the uterine carcinomas occurring as second tumors, four and seven years after radiation treatment, respectively, leads the author to think the second tumors are a consequence of the irradiation. Since such an event is extremely infrequent, it should not interfere or discourage the use of roentgen treatment; moreover, it is possible that other undetermined factors intervened in the causation of the second tumor.—*William M. Loehr, M.D.*

JARVIS, JOSEPH B. Individualizing the tumor dose in carcinoma of the uterine cervix by means of a simple caliper. *Radiology*, June, 1949, *52*, 866–868.

The author presents a simple caliper which he believes offers an accurate, rapid and convenient method of individualized treatment of carcinoma of the uterine cervix, based on actual tumor dose.

The caliper is used in the following manner: the patient is prepared for pelvic examination in the usual position. The examiner introduces the straight rod into the vagina guiding its tip to cervical os (or lesion) with the fingers of one hand. While this tip is kept in contact with the os during all measurements the other hand swings the curved rod into position on the skin surface of the abdomen at the approximate center of the treatment fields to be used, and the operator reads the distance between the opened tips, which corresponds precisely to the thickness of the tissues traversed by the incident central beam of radiation reaching the cervix.

Measurements are taken in the same positions as the patient is treated. After the desired measurements are obtained, standard depth dose tables are consulted and treatment plan based on actual tumor dose is calculated.

The author points out that external irradiation is only one of radiologist's methods and urges that this be coordinated with other methods (radium and transvaginal roentgen

therapy) in order to reach the goal of a full cancerocidal dose to the primary lesion and its advancing extensions.

He suggests that a similar caliper on a smaller scale might be useful in determination of the depth dose in other accessible orifices, such as the mouth.—*R. D. Moreton, M.D.*

RADIOISOTOPES

Cooney, James P. Psychological factors in atomic warfare. *Radiology*, July, 1949, *53*, 104–110.

While the atomic bomb is a "diabolical instrument of death and injury to men," we have no choice but to live with it. Therefore we must keep it in proper perspective and acquire a practical attitude toward it. The intense fear which both military and civilian personnel have for nuclear explosives could readily interfere with an important military mission in time of war, hence it is necessary to realize that the radiation hazards are additional to the usual hazards of war. Since radiation does add to the complexity and severity of the usual hazards, it is essential that we know about ionizing radiations if we are to survive those usual or ordinary hazards.

War is fought with the knowledge that men will be killed, and campaigns are planned with the expectation of losing a certain number of men ("acceptable hazard"). From a military standpoint, the physical danger must be evaluated against the objective to be gained; therefore, radiation hazard should be treated no differently from the usual military hazard. However, if men are more terrified by knowledge that the ground over which they walk was exposed to recent atom bomb, than they are by seeing one in ten of their buddies killed by machine gun fire, the psychological effect could offset the gain to be accomplished by nuclear weapons. "For battle discipline and military effectiveness, the dominant measure is not the hazard itself, but the soldier's estimation of the hazard." Radiation is now the most over-evaluated hazard because of the precautions taken at Operation Crossroads; those precautions were at peacetime level, and were emphasized, whereas in war conditions, they would not be possible.

In war, soldiers are exposed to many hazards other than bullets. Some of them are overemphasized, others are under emphasized. However, there are many conditions which produce like effects to radiation. Venereal disease, which tends to be under-emphasized, produces sterility. Impotence and sterility can be caused by fractures or gunshot wounds of the spine. Leukemia may be a delayed effect of radiation, but there are delayed effects of amebic dysentery, schistosomiasis and beri beri. At Eniwetok, and Bikini, deaths were due to drinking wood alcohol, drowning, truck accident and fight-incurred skull fracture. One sailor was rendered paralyzed, sterile and impotent by a cervical spine fracture sustained by diving into a shallow pool. These received little more than passing attention in the daily press, but had there been one death from radiation, it would have been on the first page of newspapers across the country.

Whereas only 5 to 15 per cent of the deaths at Hiroshima and Nagasaki were due to radiation, the emphasis has been on that group rather than on the 85 per cent due to other causes. The atomic bomb is primarily a blast weapon of war, and we must dispel the erroneous idea that the rescue work of injured will be impossible due to residual radiation. The chief destruction in Japan was from blast, heat and secondary fires; consequently fire fighting equipment and well organized rescue squads are more important than Geiger counters. Hiroshima and Nagasaki disproved the attitude that rescue squads will not be able to go into atom-bombed cities. The residual radiation from an air burst is insignificant; the significant radiation occurs in a matter of microseconds and does not extend beyond 2,000 yards. It is perfectly safe to enter a bombed area such as occurred at both those cities to rescue the injured who cannot walk—otherwise they will die in secondary fires. In case of ground or underwater burst, casualties would be less because fire and blast hazards would be decreased, although radiation hazards would be greater.

Present evidence is that if the water supply of a city is contaminated by fission products or unfissioned materials, the water would be safe to drink after passage through a modern filtration plant. It is known that at Bikini, water, which passed through the shipboard evaporators was safe for drinking.

In discussion, Dr. R. R. Newell observed that there is an unbalanced estimation of hazards in everyday life. Thus the popular opinion of poliomyelitis hazard is overevalu-

ated, since the number of people who die from that disease is very small compared with deaths from other diseases. At the other extreme, automobile accidents approach the most killing of diseases, yet deaths due to automobile accidents are so underestimated that we do much less about them than we do with regard to disease. Traffic accidents are only just below cancer as a cause for death, yet much more money is available for the attempt to control cancer than to attempt to control traffic.

He pointed out that officers in the field have the responsibility of ascertaining when and where there is greater than acceptable hazard from radiation, and of protecting the troops who have no way of achieving that knowledge. Should the commander insist on his men taking undue risks and making unwarranted sacrifice, he would destroy the confidence of his troops.

Dr. Lawrence Knox found the presentation at variance with his understanding of the risks, from presentation of Dr. Stafford Warren and asked if we are to believe that the risk of destruction is not so great as we have been led to believe.

Dr. R. S. Stone felt that the object in Dr. Cooney's presentation was not to minimize the hazards of atomic warfare from standpoint of radiation, but rather to point out that in spite of its destructiveness, the hazard of radiation is relatively small in proportion to other hazards. He felt that the problem is one of education; that we should help people understand that this is one of the hazards of war and help them understand what we know about it. We should control ourselves but also realize that we are faced with a new thing that is of great danger to the world, both from late effects and immediate destruction.—*Angus K. Wilson, M.D.*

FEITELBERG, SERGEI. Standardization of radioactive iodine. *Science*, May 6, 1949, *109*, 456–461.

This is a description of the techniques and instrumentation of standardization of I^{131} which should be available and used in the laboratories using radioactive iodine in biology and medicine. The author summarizes the results of standardizations performed in 70 different laboratories in this country on samples of equal content of I^{131}. The results present quite a dismal picture. The standard deviation is about 30 per cent; the range is from 43 to 180, about 1:4, almost in order of magnitude. Obviously, standardization is not a simple procedure. Yet it is an extremely important one. If a worker at the upper end of the frequency plot reports with certain dosage for treatment of a given disease, and a worker at the lower end makes use of this dosage information, he will give four times the effective dose and will probably exceed the therapeutic latitude, and will get deleterious results (permanent hypothyroidism, for instance, in the treatment of Graves' disease). The paper deals in detail with many of the reasons for this discrepancy in standardization. The author is quite convinced that the solution of the problem is the replacement of the highly sensitive and somewhat temperamental G-M tube by a less sensitive but more rugged and reliable instrument for purposes of standardization, such as the ionization chamber designed by Carl B. Braestrup. This instrument is described in detail. Failla's ionization chamber is also mentioned favorably.—*E. A. Addington, M.D.*

HAMILTON, JOSEPH G. The metabolism of the radioactive elements created by nuclear fission. *New England J. Med.*, June 2, 1949, *240*, 863–870.

Present-day atomic piles produce plutonium and radioactive fission products in kilogram quantities, creating protection and disposal problems for amounts of radioactive material a millionfold greater than those encountered by the radium industry in the past half century. Metabolic studies in the rat after administration of neptunium, plutonium, and 14 other radioactive isotopes show properties significantly different from radium.

Tellurium, cesium, barium, strontium, and iodine radioactive isotopes are readily absorbed by the gastrointestinal tract, and by the lungs as well. Radioactive xenon is rapidly absorbed and excreted by the lungs. Neptunium, plutonium, and several others are not appreciably absorbed by the gastrointestinal tract or lungs. After parental injection, most radioactive isotopes accumulated in the bone are eliminated very slowly from it. However, tellurium is distributed largely to the kidneys and blood, and rapidly released. Cesium is distributed promptly throughout all body tissues, and promptly excreted. Radioactive iodine accumulates in the thyroid gland.

In the skeleton, zirconium, columbium,

cerium, and element 61 accumulate particularly in endosteal and periosteal regions, and in trabecular bone. This property of concentrating in the immediate vicinity of bone marrow, in contrast to the more diffuse distribution of radium throughout the mineral structure of the skeleton, markedly enhances radiotoxicity. Search for a method of releasing plutonium deposits in bone has to date been unsuccessful.—*H. P. Brean, M.D.*

Dubbs, Clyde A. Improved apparatus for radiobiological syntheses. *Science*, June 3, 1949, *109*, 571–572.

Radioactive natural compounds, invaluable tracers for studying intermediary metabolism, are most conveniently prepared by radiobiological methods. The apparatus designed by the pioneer workers in this field are, for the most part, obsolete. The author describes in detail an apparatus with a number of advantages over the older apparatus, the greatest being the adaptability to subsequent fractionation procedures.—*E. A. Addington, M.D.*

Salter, Wm. T. A background for biological studies with radioiodine. *Science*, May 6, 1949, *109*, 453–456.

This is an essay making a plea for investigators in the field of biological studies with radioactive iodine to have a critical perspective of the value of their investigations. Nuclear physicists, biophysicists, clinicians, and various persons associated through common interest in radioiodine need to have a comprehensive view of the problems to be solved. Many of the findings of investigators in the field are entirely empiric and have no physiological value. This is partly due to the fact that the data on radioactivity have not been integrated with a supportive program of biochemical study. Much of the essay is an interesting history of iodine and how, by chance, it was found to be intimately associated with the physiology and the treatment of thyroid disease. Many isotope-physiologists are content with developing a series of data and proclaiming conclusions which were already well established in the literature decades ago by older well founded techniques. With adequate perspective two chief questions may be answered: (1) How has radioiodine improved our knowledge of iodine metabolism and of the physiology and therapy of the thyroid gland? and (2) How do the results harmonize with the past experience?—*E. A. Addington, M.D.*

Ansell, M. B., and Rotblat, J. Radioactive iodine as a diagnostic aid for intrathoracic goitre. *Brit. J. Radiol.*, Nov., 1948, *21*, 552–558.

Intrathoracic goiter is classified as toxic or non-toxic and further as total, if four-fifths or more is in the thorax; and partial, if one-half is palpable in the neck. In the thorax, it is subdivided into anterior, lateral and posterior. The differential diagnosis at these various sites is discussed. Five roentgen features of importance in the diagnosis of substernal thyroid are presented.

Radioactive iodine, I^{131}, is utilized in differentiating substernal thyroids from other substernal and mediastinal masses. The apparatus and methods employed are described in detail. The degree of accuracy in various types of thyroid disease and the factors affecting it are discussed.—*K. L. Krabbenhoft, M.D.*

Cooper, F. W., Elkin, Daniel C., Shea, Patrick C., and Dennis, E. W. The study of peripheral vascular disease with radioactive isotopes. Part II. *Surg., Gynec. & Obst.*, June, 1949, *88*, 711–718.

By measuring the rate of disappearance of radioactive sodium chloride from the muscles of an extremity, an additional method of evaluating the circulatory physiology of the extremities has been made available.

In the study of 57 normal individuals and 102 patients with peripheral vascular disturbances, curves representing the rate of disappearance of the sodium from the muscle form statistically accurate patterns.

It is believed that this method of study may offer a valuable aid in the evaluation of certain forms of therapy which are believed to enhance the circulation.—*Mary Frances Vastine, M.D.*

Simon, Norman. Suppression of gastric acidity with beta particles of P^{32}. *Science*, June 3, 1949, *109*, 563–564.

Irradiation of the gastric mucosa by roentgen rays or gamma rays of radium has suppressed gastric acidity. Such irradiation penetrates and affects not only the gastric mucosa but also adjacent organs and damage to these adjacent organs may occur if large doses of roentgen rays or gamma rays are directed to the stomach.

The author has devised a method to restrict the radiation to the gastric mucosa by coating a rubber inflated bag with radioactive phosporus, atomic weight 32. This isotope emits beta particles whose maximum range is about 8 mm. The studies were carried out on Heidenhain pouches of 5 dogs with a resultant marked decrease in the quantity of acid in the pouch secretions. The longest period of observation after irradiation in any animal was 125 days.—*E. A. Addington, M.D.*

Lawrence, John H., Low-Beer, B. V. A., and Carpender, James W. J. Chronic lymphatic leukemia. *J.A.M.A.*, June 18, 1949, *140*, 585–588.

This paper is a review of one hundred cases of chronic lymphatic leukemia treated with P^{32} beginning in 1936 and continuing until March 1, 1947. The cases were followed until September 1, 1948. Some of the patients had roentgen therapy either before or after receiving the P^{32}. Most of the roentgen therapy was directed to either enlarged lymph glands or spleen. The sex distribution of the cases was 71 per cent male and 29 per cent female.

The average age of onset in this group was fifty-three years, with the youngest case twenty years and in the oldest case the disease began at sixty years of age. One patient had a family history of blood dyscrasia, and no patient had a history of tuberculosis, although a chronic inactive tuberculosis was found in one patient at autopsy.

Following an adequate diagnostic work-up including usually a sternal puncture, the patients received, on the average, 1 to 2 millicuries of P^{32} per week for four to eight weeks or until the relief of their symptoms. No attempt being made to return the blood count to normal limits, the therapy was directed entirely toward the relief of the symptoms. The dosage was repeated whenever necessary to control the symptoms. The response to the therapy was slightly better than that seen in most of those series treated with roentgen rays alone.

At the time of writing, 33 per cent of the group had lived five or more years after the onset, and 10 per cent had lived eight or more years. These figures, of course, will be extended, since 24 of the patients are still alive.

Seventy-three patients died of lymphatic leukemia with 21 postmortem examinations. The postmortem examinations were typical of this condition with generalized infiltration of the lymph nodes, spleen, liver, and bone marrow. In none of the cases autopsied did the pathologists report aplastic bone marrow. Several patients, however, who were not autopsied showed evidence in their peripheral blood of severe marrow depression.

A few of the patients have received P^{32} for as long as ten years, but only 1 patient has received a total dose greater than 50 millicuries.

None of the patients showed evidence of radiation sickness during the therapy. This seems to be the great advantage, according to this paper, of P^{32} therapy over roentgen therapy. Also in this series, the average length of life has been prolonged slightly over that seen with roentgen therapy. The treatment is probably somewhat more convenient, both for the patient and for the doctor, than roentgen therapy.—*Everett L. Pirkey, M.D.*

MISCELLANEOUS

Hunter, F. T., Merrill, O. E., Trump, J. G., and Robbins, L. L. The protection of personnel engaged in roentgenology and radiology. *New England J. Med.*, July 21, 1949, *241*, 79–89.

A study at the Massachusetts General Hospital employing film badges and measurements of an irradiated phantom, is attempting to correlate morphologic changes in peripheral blood with radiation exposure. Contrary to generally recorded opinion, radiation scatter at 90° from a phantom subjected to fluoroscopic radiation was found to be *more* penetrating than the beam producing it. The authors believe their observation may be explained by the action of the phantom as an absorber, eliminating the softer components of the heterogeneous beam. Those scattered photons emerging from the phantom depths during fluoroscopy would be produced largely by Compton scatter. Compton-scattered photons, however, are increased in wavelength by only 0.024 Ångstrom units for 90°, a proportionately small wavelength increase, without important effect on the quality of the more penetrating components of the original beam, the soft components of which have been largely absorbed in transit through the phantom. Using fluoroscopic factors of 85 kv. (peak), 4 ma., and 1.67 mm. of aluminum filtration, side scatter was found to have a half-value layer of almost 6 mm. of aluminum.

In fluoroscopy at 85 kv. (peak), an added filtration of 3 mm. of aluminum, as compared to 1.5 mm., did not appreciably diminish screen luminescence, but did decrease patient exposure by 35 per cent, and side scatter to the examiner by 20 per cent. Increasing added filtration beyond 3 mm. produced proportionately little further attenuation. When normalized to constant screen intensity, raising the kilovoltage above 105 increases (percentage-wise) examiner dosage rate more than it decreases patient dosage rate, suggesting that optimal fluoroscopic kilovoltage lies below 105 kv. (peak). Since side scatter at 85 kv. (peak) has a half-value layer of 5.9 mm. aluminum, while the the direct beam does not reach this value until over 140 kv. (peak), and since side scatter half-value layer increases rapidly from 85 to 105 kv. (peak), it is evident that optimal fluoroscopic kilovoltage values lie closer to 85 than 105 kv. (peak).

The authors conclude that scattered radiation is sufficiently penetrating to reach bone marrow. They suggest that fluoroscopic rooms be large to minimize back scatter from ceilings and walls. It is pointed out that the open Bucky slot of the table commonly employed today transmits large amounts of scattered radiation to the operator.—*Henry P. Brean, M.D.*

Olsson, O. An easily sterilizable, flexible cassette with intensifying screens designed for x-ray examination of operatively exposed kidneys. *J. Urol.*, June, 1949, *61*, 1032–1033.

Roentgen examination of the operatively exposed kidney has been described by Åkerlund, using a film pack without intensification. The author describes a method using a specially designed thin cassette with intensifying screens such as is used in industry for the roentgen inspection of material.

The cassette which he describes is flexible, consisting of a flat rubber bag, 10 by 15 cm. It can be sterilized as easily as other surgical equipment made of rubber. The intensifying screens increase contrast and shorten exposure time.—*Rolfe M. Harvey, M.D.*

Polgar, Francis. Contrast enema in lateral recumbency; aimed gas filling of the colon. *Radiology*, July, 1949, *53*, 49–58.

The author describes his technique of examination of the colon with the roentgen-ray beam directed horizontally. In lateral recumbency the action of gravity changes the topography of the colon.

For double contrast he generally depends upon the free gas already in the colon, although artificial insufflation is occasionally used. In obese patients the supine position may be better than the lateral recumbent. He speaks about "aimed gas filling" of the colon which consists of insufflating only a small amount of air into the colon, then changing the position of the patient until the rising air accumulates in a selected segment of the colon. He does not use a secondary diaphragm and he employs low voltage for his "aimed teleroentgenograms."

Seven case reports and six figures are included.—*E. E. Seedorf, M.D.*

Tanner, W. A., and McConchie, J. E. Effect of roentgen therapy on mouse encephalitis. *Radiology*, July, 1949, *53*, 101–103.

The authors carried out a controlled experiment on mice, using Theiler's F.A. mouse encephalitis virus, for the purpose of determining the effect, if any, of roentgen treatment on animals so infected. They point out "that there is much difficulty in evaluating any treatment of acute diseases, which if they do not lead to death, usually result in recovery."

Their technique of roentgen therapy consisted of irradiation limited, in one group, to the skull, and in another group they employed total body irradiation. They first determined the toxic effect of roentgen irradiation upon mice and found that while deaths did occur at irregular intervals, they were not related to dosage of roentgen rays.

Groups of mice were then injected with mouse encephalitis virus. Controls were run on mice which were infected with varying dilutions of virus, both with and without roentgen therapy and, those with roentgen therapy, with irradiation only over the skull and irradiation over the entire body. Two groups of infected mice were irradiated daily, during the first six days following inoculation, and three groups were irradiated during a period of six to eleven days, when symptoms were expected to appear.

They found that "in terms of mortality rate, or indeed of survival time, no significant differences were observed among the several groups of irradiated animals. Neither was there any appreciable difference between control and irradiated mice."—*Angus K. Wilson, M.D.*

MOORE, ALICE E. The destructive effect of the virus of Russian Far East encephalitis on the transplantable mouse sarcoma 180. *Cancer*, May, 1949, *2*, 525–534.

The observation that viruses can parasitize tumors and in some instances interfere with tumor growth was made by Levaditi and Nicolau many years ago. The virus of Russian Far East encephalitis readily proliferates in mouse sarcoma 180 and definitely interferes with tumor growth. Its virus in high dilutions also kills mice when inoculated either intracerebrally, intraperitoneally, or subcutaneously. Peripheral systemic immunity can be produced by vaccination.

The present study shows that sublethal doses of the virus produce no effect on tumor growth. When doses sufficient to kill the mouse by encephalitis are given through intraperitoneal injection, the sarcoma is markedly inhibited or destroyed to a point where tissue transplants are unsuccessful. The virus appears first and in the highest concentration in the tumor for the first five days after inoculation. Thereafter, it is present in high and equal concentration in the tumor and brain. Virus-bearing tumor pieces, whether infected in vivo or in vitro, fail to grow, but do carry the infectious agent with them when implanted into non-immune animals. Pieces from animals ill from virus infection fail to grow when inplanted into immune animals. The cellular damage caused by the virus infection is demonstrable on section and can be confirmed by bioassay.

Although it has been proved possible to cause destruction of transplantable mouse sarcoma 180 by this virus, it has unfortunately always been associated with infection and eventual death of the animal.—*J. A. Campbell, M.D.*

SCOTT, ROGER B., and BRACK, C. BERNARD. Attempted heterologous transplantation of carcinoma of the cervix. *Bull. Johns Hopkins Hosp.*, June, 1949, *84*, 526–531.

Since successful heterologous transplantation of human carcinoma and sarcoma tissue into the anterior chamber of the guinea pig's eye was reported, this was an effort made to transplant human carcinoma of the cervix in the same manner. It was hoped that such a study would more clearly define a preponderant epidermoid cell type (spinal, transitional or basal) than even the microscope as well as perhaps lead the way toward shedding some light on the much discussed intraepithelial or carcinoma-in-situ cervical lesion.

Twelve patients with untreated carcinoma of the cervix classified as League of Nations Stage II to IV were selected. Eight adult female guinea pigs were used for each biopsy. None of the transplants were successful, however, and in only 2 instances tiny islands of viable malignant tissue were found in the eye later. These, however, proved to be of the same cell type as the biopsy specimen used.

It was concluded that the heterologous transplantation technique for the study of human malignant tissue is not applicable to carcinoma of the cervix.—*J. J. Wiesner, M.D.*

MONDOLFO, SILVANO. Investigaciones experimentales sobre la aceleración del callo óseo en las fracturas. (Experimental research on the acceleration of callus formation in bone fractures.) *Rev. ortop. y traumatol.*, July-Oct., 1949, *19*, 47–60.

The author reports on experimental work, aiming at an artificial acceleration of the process of callus formation in bone by means of injection of an alcohol extract of bone, antireticulocytotoxic serum, and total extracts of embryos. There was no resulting acceleration of callus formation in the experiments made in different species of animals, although the calluses were larger in some cases than in the control animals.—*J. A. del Regato, M.D.*

CASSEN, BENEDICT, and CURTIS, LAWRENCE. Measurement of ionizing radiations in vivo. *Science*, July 22, 1949, *110*, 94–95.

This is a description of a very ingenious type of apparatus for measuring ionizing radiations based upon their ability to produce fluorescence in certain crystals. The fluorescence is identified by a photomultiplier tube and the quantity of fluorescence can then be recorded. It has been found possible to make these recording instruments small enough to pass them through an ordinary 15 gauge hypodermic needle. The fluorescent crystals which were usually used were zinc sulphide or zinc cadmium. One of the drawbacks of the use of this apparatus was the fact that the response of the fluorescent crystals varied depending upon the wavelengths of the roentgen rays used.—*R. P. Barden, M.D.*

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